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A	Essential thrombocythaemia with cerebrovascular accident
B	Antiphospholipid syndrome with reactive thrombocytosis
C	Cerebral lupus with reactive thrombocytosis
D	Chronic myelogenous leukaemia (CML)
E	Acute myeloid leukaemia

Explanation

D Chronic myelogenous leukaemia (CML)

The history is compatible with a cerebrovascular accident, and the high platelet count is likely to be the cause. Chronic myelogenous leukaemia (a myeloproliferative disorder) usually manifests with thrombocytosis at presentation, usually with a raised white cell count that is grossly left-shifted (where promyelocytes, metamyelocytes and myelocytes are all

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You are asked to review the case of a 68-year-old woman who has had a lengthy dental procedure earlier in the day. She has a background of angina.

Current medications are isosorbide mononitrate and co-trimoxazole for a resistant urinary tract infection. She is complaining of a headache and breathlessness.

Examination shows her to be cyanosed.

Arterial blood gas on a 15 l non-rebreathe O_2 mask:

pH	7.42
P_aO_2	39.2 kPa
P_aCO_2	4.1 kPa
O_2 sats	70%
Portable chest X-ray	Normal appearance

What is the most likely diagnosis?

Your answer was correct

A Aspiration

B Carbon monoxide poisoning

C Methaemoglobinaemia

D Pulmonary embolism

E Glucose-6-phosphate dehydrogenase (G6PD) deficiency

Explanation

C Methaemoglobinaemia

Haemoglobin carries iron in its ferrous form (Fe^{2+}). When it is converted to

WCC	20 × 10⁹/l
PLT	450 × 10⁹/l
CXR	New shadowing at right base

He is diagnosed with acute chest syndrome, possibly related to mycoplasma infection.

What intervention has been shown to reduce the incidence of acute chest syndrome?

A	Low-dose enoxaparin
B	Prophylactic clarithromycin
C	Hydroxyurea
D	Folate supplements
E	Low-dose aspirin

33317

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A 24-year-old man presents with weakness of the left arm. He completed chemotherapy for diffuse large B-cell lymphoma 6 months previously. He had stage 4 disease at diagnosis, with lesions in his lungs and bone marrow at diagnosis. He received six courses of RCHOP chemotherapy (rituximab, vincristine, doxorubicin, cyclophosphamide and prednisolone) and six intrathecal injections of methotrexate; computed tomography at the end of treatment confirmed complete remission.

Examination shows power of 3/5 in the left arm biceps and triceps with decreased tone. Reflexes are reduced globally, and plantar reflexes are mute bilaterally.

Investigations:

Hb	16.3 g/dl
WCC	3.9 x 10^9/l
PLT	195 x 10^9/l
Bilirubin	9.0 µmol/l

LDH	1503 u/l (10–250)
MRI brain and spine	Unremarkable

CSF investigations:

Protein	1.3 g/l (0.15–0.45)
Cell count 6 (<5/ml)	80% lymphocytes
Culture	No growth at 48 h

What is the most likely diagnosis?

A	Guillain–Barré syndrome
B	Vincristine neuropathy
C	Methotrexate leucoencephalopathy
D	CNS relapse of lymphoma

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Cell count 6 (<5/ml)	80% lymphocytes
Culture	No growth at 48 h

What is the most likely diagnosis?

Your answer was incorrect

Question 1 of 139

D	CNS relapse of lymphoma

Central nervous system relapse is not uncommon in high-grade lymphoma, particularly if risk factors are present (more than one site of extranodal disease, high lactate dehydrogenase, bone marrow or sinus involvement). Presentation is often initially occult, with no lesion demonstrated on imaging, and several lumbar punctures may be necessary with samples examined by the technique of cytospin, which concentrates cellular material to increase the sensitivity of cytology. Clinical signs are often complicated by the fact that reflexes are suppressed from vincristine exposure. Central nervous system (CNS) lymphoma carries a grave prognosis, but if remission can be induced by high-dose cytosine arabinoside or high-dose methotrexate with folinic acid rescue, then autologous stem cell transplantation or cranial radiotherapy can be effective.

B	Vincristine neuropathy

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B Vincristine neuropathy

Vincristine neuropathy is progressive, beginning with peripheral sensory loss, rather than the picture seen here.

A Guillain–Barré syndrome

Guillain–Barré syndrome is associated with ascending weakness, which usually begins some 2–3 weeks after a viral illness.

C Methotrexate leucoencephalopathy

Methotrexate leukoencephalopathy is most commonly seen between 2 and 14 days of administration, with symptoms developing over minutes to hours, characterised by headache and progressive deterioration in conscious level accompanied by seizures and later focal neurological deficit. It is more commonly seen in children and is associated with white matter attenuation on CT scanning.

A 72-year-old man presents to the clinic with fever, weight loss, lethargy and a sensation of pins and needles in his feet. He is particularly concerned that he has begun to suffer increasing headaches over the past few weeks.

Other past history of note is gout, which developed a few months ago.

On examination, there are lymphadenopathy and hepatosplenomegaly.

Investigations:

Hb	9.8 g/dl (normal MCV)
WCC	4.1 × 10^9/l
PLT	95 × 10^9/l
Na^+	141 mmol/l
K^+	5.1 mmol/l
Creatinine	145 µmol/l
ESR	75 mm/h
IgM	Paraprotein band

Creatinine	145 µmol/l
ESR	75 mm/h
IgM	Paraprotein band
Bone marrow	Plasma cell infiltration

Which of the following is the most likely diagnosis?

A	Chronic lymphocytic leukaemia (CLL)
B	Waldenström’s macroglobulinaemia (WM)
C	Acute lymphoblastic leukaemia (ALL)
D	Myelofibrosis
E	Myelodysplasia

B Waldenström's macroglobulinaemia (WM)

The combination of anaemia with low white cell and platelet counts, raised ESR, plasma cell infiltration of bone marrow and IgM paraprotein band is highly suggestive of Waldenström's. Death occurs either due to cardiovascular events because of increased viscosity, or due to progression of bone marrow infiltration leading to suppressed response to infection. Frontline chemotherapy for Waldenström's includes the use of alkylating agents; for patients who suffer from acute manifestations of hyperviscosity syndrome, plasmapheresis is the treatment of choice.

A Chronic lymphocytic leukaemia (CLL)

CLL is associated with splenomegaly, although the predominant abnormality seen is a rise in peripheral blood white

count.

C	Acute lymphoblastic leukaemia (ALL)

ALL is usually associated with severe anaemia and thrombocytopenia, with recurrent infections and bleeding episodes, rather than the picture seen here.

D	Myelofibrosis

Myelofibrosis is not associated with symptoms of hyperviscosity (the neuropathy and headaches seen here).

E	Myelodysplasia

Like myelofibrosis, myelodysplasia is not associated with the hyperviscosity symptoms reported here.

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A 50-year-old man with aggressive lymphoma is receiving combination chemotherapy with rituximab, cyclophosphamide, vincristine, doxorubicin and prednisolone. At the start of therapy he had several cervical and axillary lymph nodes, none larger than 2 cm. Several studies of investigational products are available, and he asks you about the terminology of drug development.

In terms of the process of researching a new drug in the oncology setting, which of the following best applies to phase I studies?

A The aim of a phase I study is to assess initial therapeutic activity

B Phase I studies are conducted once an initial therapeutic effect in humans is demonstrated

C It is common to combine

In terms of the process of researching a new drug in the oncology setting, which of the following best applies to phase I studies?

A The aim of a phase I study is to assess initial therapeutic activity

B Phase I studies are conducted once an initial therapeutic effect in humans is demonstrated

C It is common to combine phase I and II studies

D Phase I studies usually recruit several hundred patients

E Phase I studies are classically randomised controlled and double-blinded

C It is common to combine phase I and II studies

Phase I studies study safety, pharmacokinetics and pharmacodynamics, whereas phase II studies study whether there is a therapeutic response. These two phases, in practice, are often combined.

A The aim of a phase I study is to assess initial therapeutic activity

Phase II studies assess whether or not there is a therapeutic response, whereas phase I studies assess safety, pharmacokinetics and pharmacodynamics (which may include initial hints as to the efficacy of the intervention).

B Phase I studies are conducted once an initial therapeutic effect in humans is demonstrated

Phase III studies are performed once initial safety and efficacy evaluation is completed, and usually compare the drug with an alternative.

D Phase I studies usually recruit several hundred patients

Phase I studies study safety, pharmacokinetics and pharmacodynamics in an investigational agent’s first usage in human subjects. They are not designed to assess therapeutic response, and patients should be aware of this as part of the consent process. As such, they tend to be small trials with only a few patients recruited to them.

E Phase I studies are classically randomised controlled and double-blinded

Usually phase III and sometimes phase II trials are randomised controlled trials. Within the oncology trial setting, sponsors do not need to be blinded. They can be privy to all information

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A	Two units of HLA (human leucocyte antigen) matched blood from a family member

Non-CMV-screened blood runs the risk of transmission of CMV, and lack of irradiation runs the risk of the unit containing viable

B	Two units of ABO matched blood from a family member

Because of previous transfusions, the likelihood of mismatching and a subsequent transfusion reaction is very high.

C	Two units of standard cross-matched blood

This runs the risk of HLA mismatch, the presence of T cells in the donor sample and CMV infection.

6381

4G 12:16

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You are called to see a 40-year-old woman who has become acutely short of breath, although she denies specific chest pain. She had a total knee replacement the previous day, which was uncomplicated. In the notes it is documented that she had a non-haemolytic febrile reaction this morning during a single-unit blood transfusion, which responded rapidly to hydrocortisone and chlorpheniramine. She has received no additional intravenous fluids. She has no previous medical history of note. She works part-time as an aerobics instructor and has four children. She does not smoke.

On examination, she is acutely short of breath, with a respiratory rate of 45 breaths per minute at rest. She is using accessory muscles and is clearly exhausted. Auscultation of the chest reveals widespread crackles. She has expectorated a small amount of frothy sputum. She is afebrile, blood pressure 150/90 mmHg, pulse 130 regular. Electrocardiogram shows no evidence of acute ischaemia. Chest X-ray shows

Electrocardiogram shows no evidence of acute ischaemia. Chest X-ray shows widespread alveolar shadowing. Heart size is normal. Full blood count and renal function are normal.

What is the most likely diagnosis?

A	Transfusion-related acute lung injury (TRALI)
B	Acute pulmonary oedema due to fluid overload from rapid infusion of blood products
C	Hospital-acquired pneumonia
D	Massive pulmonary embolus
E	Adult respiratory distress syndrome due to overwhelming sepsis

8250

A Transfusion-related acute lung injury (TRALI)

This lady has a classic history for transfusion-related acute lung injury (TRALI): she is multiparous, had a transfusion reaction and has developed adult respiratory distress within 6 h of a blood transfusion – this is thought to be due to anti-HLA or anti-neutrophil antibodies (hence is more common in multiparous women, and particularly donors rather than recipients).

The condition is diagnosed clinically and is thought to be significantly underdiagnosed. Treatment is with full respiratory support, as the condition is reversible after a few days. The diagnosis can be confirmed by the finding of anti-HLA or anti-neutrophil antibodies in the donor or recipient. Donors who carry such antibodies are resigned from the donor pool.

When recipients who have developed TRALI require further transfusion, male donors can be used to reduce the risk

12:18

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donors can be used to reduce the risk of subsequent attacks. This is because they have a much lower rate of carriage of anti-HLA or anti-neutrophil antibodies (1–5% vs up to 20% in women).

B	Acute pulmonary oedema due to fluid overload from rapid infusion of blood products

There is no history of the one unit of blood being rapidly transfused. One unit of packed red cells is approximately 300 ml of fluid. Considering that the patient is young, fit and otherwise healthy, it would be unusual to get fluid overload from such a small amount of fluid.

C	Hospital-acquired pneumonia

Despite her shortness of breath and tachycardia, this patient has no other signs of sepsis or infection. Hospital-acquired pneumonias are diagnosed once a patient has been in a healthcare

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once a patient has been in a healthcare setting for 5 days or more, which is not the case here.

D	Massive pulmonary embolus

This patient has a high heart rate, recent surgery and breathlessness, but she is maintaining a normal blood pressure and has widespread crackles on her lungs. In a massive PE, a patient would usually become haemodynamically compromised.

E	Adult respiratory distress syndrome due to overwhelming sepsis

Although this patient does have evidence of acute respiratory distress syndrome, there are no other signs of sepsis or infection. Her ARDS is due to TRALI.

8250

Question 6 of 139

A 50-year-old woman presents with lethargy and easy bruising. She was treated with curative intent for early stage breast cancer 5 years ago and has been well since. She is on no medication. There is no other significant previous medical history.

Examination shows a thin woman with bruises on all extremities and pale conjunctiva but is otherwise normal.

Investigations:

Hb	9.9 g/dl
WCC	3.5 × 10⁹/l
PLT	113 × 10⁹/l
Neutrophils	1.0 × 10⁹/l
Reticulocytes	13 × 10⁹/l (25-85)
PT	12 s (11.5-15.5)
APTT	35 s (30-40)
Blood film	Band forms, myelocytes and occasional promyelocytes, as

Blood film	Band forms, myelocytes and occasional promyelocytes, as well as nucleated red blood cells

What diagnosis would best fit this picture?

A	Acute promyelocytic leukaemia
B	Secondary breast cancer
C	Myelofibrosis
D	Thrombotic thrombocytopenic purpura
E	Aplastic anaemia

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12:22

Question 6 of 139

has been well since. She is on no medication. There is no other significant previous medical history.

Examination shows a thin woman with bruises on all extremities and pale conjunctiva but is otherwise normal.

Investigations:

Hb	9.9 g/dl
WCC	3.5 × 10⁹/l
PLT	113 × 10⁹/l
Neutrophils	1.0 × 10⁹/l
Reticulocytes	13 × 10⁹/l (25-85)
PT	12 s (11.5-15.5)
APTT	35 s (30-40)
Blood film	Band forms, myelocytes and occasional promyelocytes, as well as nucleated red blood cells

What diagnosis would best fit this

B Secondary breast cancer

The patient's blood tests show leuco-erythroblastic anaemia (left-shifted granulocytic series and nucleated red blood cells) with pancytopenia. This can be seen with high bone marrow turnover, e.g. in severe haemolytic anaemia (but the reticulocyte count will be high), myelofibrosis and chronic myeloid leukaemia (where there will be splenomegaly and the white cell and platelet count will usually be raised) or bone marrow invasion. Often in bone marrow invasion the invading malignancy will already have been diagnosed previously. The diagnosis requires a bone marrow trephine, which will usually show replacement of haematopoietic tissue with malignant cells.

E Aplastic anaemia

Aplastic anaemia is associated with peripheral pancytopenia and marrow failure.

A	Acute promyelocytic leukaemia

Acute promyelocytic leukaemia is characterised by the presence of promyelocytes in peripheral blood, rather than the leuco-erythroblastic blood picture seen here.

C	Myelofibrosis

Myelofibrosis does reveal a leucoerythroblastic blood picture, but given the history of lumpectomy, secondary breast cancer is a more likely cause.

D	Thrombotic thrombocytopenic purpura

TTP is associated with increased risk of thrombosis, haemolysis and a low platelet count.

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A 43-year-old man presents to the Emergency department with a fever of 38.9 °C. He had finished a third cycle of chemotherapy for osteosarcoma only a few days earlier and he has an indwelling central venous catheter.

On examination, he looks unwell, he has a fever of 38.9 °C and his BP is 100/70 mmHg, with pulse 95/min and regular. There are no signs of pharyngitis and only minor erythema around the exit site for his catheter.

Investigations:

Hb	10.4 g/dl
WCC	5.4 x 10^9/l
Neutrophils	0.2 x 10^9/l
PLT	125 x 10^9/l
Na^+	138 mmol/l
K^+	4.3 mmol/l
Creatinine	122 µmol/l

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Creatinine	122 µmol/l
ALT	174 U/l
ALP	392 U/l
Albumin	26 g/l

Which of the following is the most appropriate antibiotic regimen?

A Gentamicin, piperacillin/tazobactam, vancomycin

B Piperacillin/tazobactam, gentamicin, amphotericin

C Gentamicin, vancomycin, flucloxacillin

D Gentamicin, vancomycin, flucloxacillin, tazobactam

E Amphotericin B, gentamicin, flucloxacillin

A	Gentamicin, piperacillin/tazobactam, vancomycin

This patient has febrile neutropenia, having recently completed a course of chemotherapy, and with an indwelling vascular catheter. Hence a broad-spectrum antibacterial regimen, including adequate staphylococcal cover, is recommended. Therapy is not delayed whilst awaiting sample results, and anti-fungal therapy is usually considered later if non-response to therapy is seen. The alkaline phosphatase elevation seen here may be due to hepatic dysfunction or. of course, related to the underlying bony tumour.

B	Piperacillin/tazobactam, gentamicin, amphotericin

This option sacrifices adequate anti-staphylococcal cover for introduction of an anti-fungal. In practice anti-fungals are introduced in the event that a response to therapy is not seen

that a response to therapy is not seen at 48 h.

C	Gentamicin, vancomycin, flucloxacillin

Piperacillin/tazobactam is the cornerstone of therapy according to **NICE guidelines**. It must therefore be included here.

D	Gentamicin, vancomycin, flucloxacillin, tazobactam

This option doesn't include piperacillin, meaning that it doesn't conform with current NICE guidelines.

E	Amphotericin B, gentamicin, flucloxacillin

Although this option provides good cover for staphylococcal and fungal pathogens, it fails to provide adequate cover against other potential infective agents.

You are asked to see a 60-year-old man on the High Dependency Unit. He underwent coronary artery bypass 7 days ago and has developed some necrotic ulcers on his abdominal wall. He has had two myocardial infarctions in the last year. He was otherwise recovering well post-operatively. He is on intravenous unfractionated heparin, aspirin, atenolol and lisinopril.

Examination shows a breathless, cyanosed man, with tachycardia and a clear chest. His BP is 110/60 mmHg. His left leg is swollen and mottled. Chest X-ray is clear.

Blood tests show:

Hb	10.3 g/dl
WCC	5.3 x 10^9/l
PLT	25 x 10^9/l
Blood film	Confirms low PLT
APTT	42 s (30–40s)

How will you manage this patient?

APTT	42 s (30-40s)

How will you manage this patient?

A	Give a unit of platelets
B	Change to low-molecular weight heparin
C	Stop all anticoagulation until the platelet count returns to normal
D	Stop heparin and start anticoagulation with danaparoid until the platelet count returns to normal
E	Stop heparin and start anticoagulation with warfarin, once a thrombophilia test has ruled out protein C or S deficiency

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D Stop heparin and start anticoagulation with danaparoid until the platelet count returns to normal

This patient has low platelets and necrotic skin lesions. Low platelets in association with heparin therapy are associated with heparin-induced thrombocytopenia with thrombosis (HIT type II). The skin lesions are due to heparin-induced skin necrosis. HIT type I is a non-immune condition which occurs with 5 days of starting heparin, and the platelet count rarely falls below 100 10^9/l. HIT type II, also known as heparin-induced thrombocytopenia with thrombosis, presents with a >50% fall in the platelet count and is associated with a very high incidence of venous thromboembolism. In patients newly treated with heparin the condition takes 7 days to develop, but in patients who have previously received heparin the condition can come on within 24 h. The diagnosis is established by confirming the presence of antibodies

the condition can come on within 24 h. The diagnosis is established by confirming the presence of antibodies to heparin bound to co-factor 4, usually by enzyme-linked immunosorbent assay. Treatment is with immediate withdrawal of all heparin, including heparin flushes for indwelling cannulae.

Low-molecular weight heparin will cross-react in most cases, although it carries a lower risk of causing the condition *de novo*. Because of the high incidence of thrombosis (20–50%), alternative anticoagulation with the heparinoid danaparoid (a combination of heparan and dermatan sulphate) or lepirudin (a recombinant direct thrombin inhibitor) should be used in all patients until the platelet count returns to normal. Over the longer term, non-heparin-based anticoagulation (e.g. with lepirudin or a factor Xa inhibitor) may be the better option.

A Give a unit of platelets

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A Give a unit of platelets

Thrombosis which occurs in HIT type 2 is antibody mediated, and thus giving a unit of platelets and continuing heparin runs the risk of further thrombosis occurring.

B Change to low-molecular weight heparin

Although the risk of HIT occurring is lower with low-molecular weight heparin, a switch to non-heparin-based anticoagulation must still be made.

C Stop all anticoagulation until the platelet count returns to normal

Given the likelihood of a DVT and subsequent pulmonary embolus, continuing anticoagulation using a non-heparin-based agent is essential.

E Stop heparin and start anticoagulation with warfarin

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A 50-year-old painter who specialises in house restoration goes to see a new GP for a routine signing-on medical.

Past medical history of note includes a recent diagnosis of gout. Some blood tests are arranged, and the GP mails you to discuss the results. He reports on his e-mail that the clinical examination was unremarkable.

Investigations:

Hb	10.5 g/dl
MCV	60 fl
WCC	5.0 x 10^9/l
PLT	190 x 10^9/l
Ferritin	300 µmol/l (15-300)
Hb electrophoresis	Normal

Which of the following is the most likely diagnosis?

PLT	190 x 10^9/l
Ferritin	300 µmol/l (15-300)
Hb electrophoresis	Normal

Which of the following is the most likely diagnosis?

A Iron deficiency anaemia

B Beta-thalassaemia

C Anaemia of chronic disease

D Lead poisoning

E Porphyria

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D Lead poisoning

The clue given here is in his occupation as a painter. It is still possible, even in the days of lead-free paints, that he would have had significant lead exposure while stripping the walls in old houses. The blood picture of lead toxicity mimics that seen with iron deficiency anaemia; additionally, disordered handling of uric acid may lead to the development of gout.

B Beta-thalassaemia

The normal Hb electrophoresis and lack of description of an ethnic origin consistent with thalassaemia counts against this as a diagnosis.

A Iron deficiency anaemia

Although iron deficiency anaemia does present with microcytic anaemia, the normal ferritin level would be very unusual in this context.

A Iron deficiency anaemia

Although iron deficiency anaemia does present with microcytic anaemia, the normal ferritin level would be very unusual in this context.

C Anaemia of chronic disease

Anaemia of chronic disease is normally associated with a normochromic, normocytic blood picture.

E Porphyria

Cutaneous porphyrias are associated with a skin rash not seen here, and acute porphyrias are associated with paroxysms of acute psychiatric disturbance with hypertension, tachycardia and hyponatraemia.

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A 24-year-old man of Indian ethnic origin is referred for investigation of anaemia by his GP. He is asymptomatic and attended the surgery for new patient blood testing. He has no physical complaints.

Examination is unremarkable.

Investigations:

Full blood count:

Hb	12.5 g/dl (13.5–18.0)
WBC	6.8 × 10^9/l (4.0–11.0)
PLT	340 × 10^9/l (150–450)
MCV	65 fl (78–100)

Haemoglobin electrophoresis:

HbA	91.7% (95–98)
HbA_2	7.1% (2.0–3.0)
HbF	1.2% (1.0–2.0)
Other protein bands	None seen

What is the most likely diagnosis?

Question 10 of 139

Haemoglobin electrophoresis:

HbA	91.7% (95–98)
HbA_2	7.1% (2.0–3.0)
HbF	1.2% (1.0–2.0)
Other protein bands	None seen

What is the most likely diagnosis?

A Alpha-thalassaemia trait

B Haemoglobin H disease

C Beta-thalassaemia minor

D Beta-thalassaemia major

E Sickle cell trait

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C Beta-thalassaemia minor

Loss of one beta-globin gene results in a mild reduction in normal HbA (2 × alpha- and 2 × beta-globins) production and a compensatory increase in HbA2 production (2 × alpha- and 2 × delta-globins). These patients are asymptomatic with normal examinations and are often not diagnosed until routine bloods detect a mild anaemia and microcytosis.

Haemoglobin is made up of haem (iron-containing compound that binds oxygen) and globin (protein components that bind to and wrap around haem). The majority (95–98%) of adult haemoglobin is made up of HbA (2 × alpha-globins and 2 × beta-globins). A small percentage (2–3%) of adult haemoglobin is HbA2 (2 × alpha-globins and 2 × delta-globins). Adults usually have only a small amount of fetal haemoglobin or HbF (2 × alpha-globins and 2 × gamma-globins). Thalassaemia is a haemoglobinopathy resulting from defective synthesis of globin chains that prevents normal

Thalassaemia is a haemoglobinopathy resulting from defective synthesis of globin chains that prevents normal haemoglobin production and function. There are two genes on each chromosome 16 coding for alpha-globins (four in total), and one gene on each chromosome 11 coding for beta-globins (two in total). Phenotype depends on the number of deleted or mutated genes coding for the corresponding globin.

A	Alpha-thalassaemia trait

Alpha-thalassaemia trait is a result of mutations in two out of the four globin genes. This causes an asymptomatic microcytic anaemia as seen in this case. However, because alpha-globin is present in HbA2 in addition to HbA, you would not find an increase of HbA2 (2 × alpha- and 2 × delta-globins) detected in haemoglobin electrophoresis as seen here. See overall explanation for an overview of thalassaemia.

B	Haemoglobin H disease

Haemoglobin H disease is a result of mutations in three out of the four alpha-globin genes. HbH refers to a very abnormal haemoglobin consisting of four beta-globins. As this is an ineffective haemoglobin, it would cause a more significant and symptomatic anaemia with signs of this on examination. Furthermore, haemoglobin electrophoresis would identify HbH as a separate band and the HbA2 percentage would not be raised, as this requires functioning alpha-globins. See overall explanation for an overview of thalassaemia.

D	Beta-thalassaemia major

Beta-thalassaemia major is a result of mutations in both beta-globin genes resulting in no functioning beta-globin and therefore no HbA. Therefore this presents in childhood with severe, transfusion-dependent microcytic anaemia. Beta-thalassaemia major is not usually apparent at birth due to

A 30-year-old male nurse presents with prolonged bleeding after a routine dental extraction. It is two days since the procedure, and the bleeding has been continuous: he has noticed black stools on three separate occasions.

Past medical history includes a postoperative haemorrhage following tonsillectomy, that required a blood transfusion. He has one brother who is well, and believes a cousin may have died of bleeding during childbirth.

On examination, he is pale but well perfused. Rectal examination confirms melaena.

Investigations:

Hb	8.1 g/dl
PT	28 s (11.5–15.5)
Activated PTT	33 s (30–40)
Fibrinogen	2.3 g/l (1.8–5.4)
Mixing studies with	normal plasma shows complete correction

Fibrinogen	2.3 g/l (1.8–5.4)
Mixing studies with 50;50 test	normal plasma shows complete correction of PT

What diagnosis should be considered at this stage pending further investigation?

A Inherited Factor IX deficiency

B Self-dosing with warfarin

C Acquired Factor IX deficiency

D Inherited Factor VII deficiency

E Acquired Factor VII deficiency

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perfused. Rectal examination confirms melaena.

Investigations:

Hb	8.1 g/dl
PT	28 s (11.5–15.5)
Activated PTT	33 s (30–40)
Fibrinogen	2.3 g/l (1.8–5.4)
Mixing studies with 50;50 test	normal plasma shows complete correction of PT

What diagnosis should be considered at this stage pending further investigation?

Your answer was incorrect

A	Inherited Factor IX deficiency
B	Self-dosing with warfarin

Question 11 of 139

D Inherited Factor VII deficiency

Factor VII is the only factor unique to the prothrombin time (PT), and deficiency of Factor VII therefore gives a prolonged PT and normal APTT. Deficiencies of II, V and X will prolong both activated partial thromboplastin time (APTT) and PT. Deficiencies of XII, XI, IX and VIII will prolong APTT alone. When an abnormality is detected in the PT/APTT, the studies are repeated with a 50:50 mix of test and normal plasma: straightforward factor deficiencies will correct with mixing, but inhibitors (most commonly lupus anticoagulant) do not correct.

A Inherited Factor IX deficiency

Factor IX deficiency results in prolongation of APTT, and would correct with normal plasma mixing.

B Self-dosing with warfarin

Given that other family members have

A 77-year-old man presents to the clinic with extreme tiredness. He also complains of petechiae, bruising and has had a couple of nose bleeds over the past few months.

On examination, you confirm bruising and petechiae; he also looks generally pale and there is splenomegaly on abdominal examination.

Investigations:

Hb	8.9 g/dl
MCV	104 fl
WCC	3.8 x 10^9/l
PLT	112 x 10^9/l
Na^+	140 mmol/l
K^+	5.0 mmol/l
Creatinine	140 μmol/l

Which of the following is the best way to confirm the diagnosis?

A Erythropoietin levels

WCC	3.8 x 10⁹/l
PLT	112 x 10⁹/l
Na^+	140 mmol/l
K^+	5.0 mmol/l
Creatinine	140 µmol/l

Which of the following is the best way to confirm the diagnosis?

A Erythropoietin levels

B B_{12} levels

C Bone marrow biopsy

D Bone marrow aspiration

E Ferritin levels

21032

1:22

Question 12 of 139

This man potentially has myelodysplasia or myelofibrosis, and a bone marrow biopsy is therefore the most logical next step. Typical bone marrow biopsy in myelofibrosis reveals non-uniform areas of reticular fibrosis interspersed with some areas of increased cellularity. In myelodysplasia there is an increase in the megakaryocyte component of bone marrow, and cells may be abnormally small or large, containing cytogenetic abnormalities.

A	Erythropoietin levels

EPO levels are most useful in differentiating primary and secondary polycythaemia (due to chronic tissue hypoxia).

B	B_{12} levels

B_{12} levels may be reduced, although B_{12} deficiency doesn't fit with the splenomegaly seen here.

1:22

Question 12 of 139

A Erythropoietin levels

EPO levels are most useful in differentiating primary and secondary polycythaemia (due to chronic tissue hypoxia).

B B_{12} levels

B_{12} levels may be reduced, although B_{12} deficiency doesn’t fit with the splenomegaly seen here.

D Bone marrow aspiration

Trephine is preferred to demonstrate the abnormal bone marrow architecture seen in patients with myelodysplastic syndrome.

E Ferritin levels

Iron deficiency anaemia is associated with microcytic anaemia rather than the macrocytosis and splenomegaly seen here.

21032

A 20-year-old woman, who is taking the oral contraceptive pill, presents with pleuritic chest pain of sudden onset. She has recently flown back to this country from Australia. She has no family history of venous thromboembolism. She is a full-time mother of two children, aged 3 and 6. Her only medication is the oral contraceptive pill.

Examination shows her to be breathless, cyanosed and in distress. She is tachycardic, with a blood pressure of 110/70 mmHg and a loud pulmonary component of the second heart sound. There is a pleural rub, with a respiratory rate of 35 breaths/min. Chest X-ray is clear.

Results below:

$p(O_2)$	7.9 kPa (11.3–12.6)
$p(CO_2)$	3.5 kPa (4.7–6.0)
Factor V Leiden (FVL) mutation	Heterozygous

She responds promptly to high-flow oxygen and low-molecular-weight (LMW) heparin. A ventilation/perfusion scan shows multiple mismatched perfusion defects.

She agrees to switch to a different mode of contraception.

Which of the following options would be the best option for management?

A	Lifelong warfarin
B	Warfarin for at least 3 months
C	LMW heparin for 3 months
D	Warfarin for 6 months and LMW heparin for future long flights
E	Warfarin for 6 months and low-dose aspirin for future long flights

Question 13 of 139

A 20-year-old woman, who is taking the oral contraceptive pill, presents with pleuritic chest pain of sudden onset. She has recently flown back to this country from Australia. She has no family history of venous thromboembolism. She is a full-time mother of two children, aged 3 and 6. Her only medication is the oral contraceptive pill.

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Factor V Leiden (FVL) mutation	Heterozygous

B Warfarin for at least 3 months

FVL is a common polymorphism, found in 2–15% of the population, and carries a 3- to 8-fold relative risk for venous thromboembolism (VTE). The mutation is synergistic with use of the oral contraceptive pill, increasing the rate of VTE in this patient group by a factor of 30, but it has been estimated that 2 million women would need to be screened to prevent one death from VTE, so routine screening is not recommended. Most studies do not show an increased risk of VTE in FVL, compared with negative controls, when patients are not taking the combined oral contraceptive pill, so there is no indication for prolonged or intensified anticoagulation, although she should review her contraceptive arrangements. As such, 3 months of warfarin therapy would be sufficient for this provoked VTE if an alternative method of contraception is sought. If the patient elects to continue the oral contraceptive pill, expert opinion is that extending the duration of

that extending the duration of anticoagulation to 6 months continues to reduce the risk of recurrent VTE.

Cascade screening of adult family members is appropriate, and members who carry FVL mutation can receive lifestyle counselling regarding contraception and long journeys. Proteins C and S, antithrombin III and activated protein C resistance are all affected by recent thrombosis and/or anticoagulation, and testing for these should be delayed until a month after all anticoagulation has ceased.

A Lifelong warfarin

Lifelong anticoagulation would be considered for recurrent VTE despite discontinuation of the oral contraceptive pill.

C LMW heparin for 3 months

Although the duration of 3 months is correct for this provoked VTE, providing oral contraception is

stopped, the mode of anticoagulation is not best practice. LMW heparin would only be continued past the initial treatment phase in pregnancy, malignancy or allergies to all oral anticoagulants.

D Warfarin for 6 months and LMW heparin for future long flights

There is no evidence that this patient will be at an increased risk of VTE once the oral contraceptive pill is discontinued. As such, prophylaxis with LMW heparin is not warranted.

E Warfarin for 6 months and low-dose aspirin for future long flights

There is no evidence that use of low-dose aspirin is effective in preventing episodes of VTE.

71440

Rate this question:

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A 72-year-old man presents with headaches, lethargy and severe intractable back pain. He also recently suffered left lower lobe pneumonia.

Over the past few days, his problems have significantly worsened and he is now unable to keep any food or fluids down and is vomiting several times during the day.

On examination, his BP is 162/95 mmHg and he looks pale. His pulse is 90/min and regular and there are bilateral crackles on auscultation of the chest.

Investigations:

Hb	10.1 g/dl
WCC	4.9 × 10^9/l
PLT	147 × 10^9/l
Na^+	142 mmol/l
K^+	6.0 mmol/l
Creatinine	890 µmol/l
Viscosity	2.78 mPa/s (1.50–1.72)

2:20

Question 14 of 139

Total protein	110 g/l
Albumin	30 g/l
P-ANCA	+
Urine	Protein++
USS renal tract	Bilateral normal-sized kidneys, no obstruction

Which of the following is the most likely diagnosis?

A	Multiple myeloma
B	Granulomatosis with polyangiitis
C	Polyarteritis nodosa
D	Anti-glomerular basement membrane (GBM) disease
E	Waldenström’s macrogammaglobulinaemia

Question 14 of 139

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Over the past few days, his problems have significantly worsened and he is now unable to keep any food or fluids down and is vomiting several times during the day.

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WCC	4.9 × 10^9/l
PLT	147 × 10^9/l
Na^+	142 mmol/l
K^+	6.0 mmol/l
Creatinine	890 µmol/l
Viscosity	2.78 mPa/s (1.50–1.72)
Total	

Question 14 of 139

A	Multiple myeloma

Whilst we are not given a serum calcium result here, the clinical history of severe backpain, headaches, lethargy and an episode of sepsis is typical of myeloma. The clinical findings of decreased serum albumin, marked elevation in total protein and proteinuria further support the diagnosis. Serum electrophoresis is likely to reveal a paraprotein band. Slightly confusingly, p-ANCA positivity is associated with both multiple myeloma and vasculitis. A period of dehydration associated with the pneumonia may well have been enough to precipitate acute on chronic kidney disease here.

B	Granulomatosis with polyangiitis

Granulomatosis with polyangiitis is associated with positive c-ANCA. P-ANCA positivity is associated with multiple myeloma.

unexpected in the absence of evidence of haematuria.

D	Anti-glomerular basement membrane (GBM) disease

Anti-GBM disease is associated with pulmonary haemorrhage and glomerulonephritis, rather than the picture here of acute on chronic kidney disease with proteinuria.

E	Waldenström’s macrogammaglobulinaemia

Waldenström’s is associated with an IgM paraprotein band as well as features of hyperviscosity syndrome and cryoglobulinaemia. Although this patient has headaches there are no other features to suggest Waldenstrom’s such as ischaemic symptoms due to hyperviscosity or cryoglobulinaemia.

21435

Rate this question: ⊖ ★★★★★

Question 15 of 139

A 40-year-old man is admitted to a Surgical Day Ward with a mild haematemesis and is awaiting endoscopy when he suffers a massive haematemesis and loses consciousness.

On examination, he is cool to the touch, with a tachypnoeic pulse of 140 beats per minute (bpm) and blood pressure 60/30 mmHg. He has already had blood taken for group-and-save that day.

Investigations:

Hb	10.5 g/dl
WBC	10 × 10^9/l
PLT	520 × 10^9/l

What is the most suitable fluid to give in the first instance?

A	Crystalloid such as normal saline
B	Group O rhesus-negative

Question 15 of 139

Investigations:

Hb	10.5 g/dl
WBC	$10 \times 10^9/l$
PLT	$520 \times 10^9/l$

What is the most suitable fluid to give in the first instance?

A	Crystalloid such as normal saline
B	Group O rhesus-negative packed red cells
C	Group-specific packed red cells
D	Fully cross-matched packed red cells
E	Immediate spin cross-matched packed red cells

A Crystalloid such as normal saline

The priority in this situation is maintenance of perfusion – the patient will die of shock before they die of anaemia – and crystalloid is likely to be readily available.

B Group O rhesus-negative packed red cells

Small stocks of group O rhesus-negative blood are kept at theatres, accident and emergency and obstetrical departments, but are only required when the patient's blood group is unknown.

C Group-specific packed red cells

Blood grouping takes 10 min, so group-specific blood can usually be issued early on in an ongoing massive haemorrhage.

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A 35-year-old man is referred to the clinic by his general practitioner. He gives a 12-month history of intermittent night sweats, weight loss, itching and chronic cough. There is no significant reported GI disturbance.

Most recently, he has noticed increasing shortness of breath on climbing the stairs, and has been suffering from an urticarial rash.

Investigations:

Eosinophils	3.0 × 10^9/l (0.04–0.4) or greater on 3 occasions in the last year
Creatinine	128 μmol/l
ANCA	-
CXR	Interstitial infiltrates and small bilateral pleural effusions
Echocardiogram	Suggestive of restrictive cardiomyopathy

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CXR	Interstitial infiltrates and small bilateral pleural effusions
Echocardiogram	Suggestive of restrictive cardiomyopathy
IgE	Raised

Which of the following is the most likely diagnosis in this case?

A Churg-Strauss syndrome

B Hyper-eosinophilic syndrome

C Acute eosinophilic pneumonia

D Chronic pulmonary eosinophilia

E Chronic parasitic infection

18549

Question 16 of 139

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Creatinine	128 µmol/l
ANCA	-
CXR	Interstitial infiltrates and small bilateral pleural effusions
Echocardiogram	Suggestive of restrictive cardiomyopathy
IgE	Raised

B Hyper-eosinophilic syndrome

This is a myeloproliferative disorder of unknown cause and is rare, occurring most commonly in men in the 30–40-year-old age group. It is associated with a persistent and markedly raised peripheral blood eosinophil count. Lung involvement may occur, as may cardiovascular involvement with fibrosis and restrictive cardiomyopathy, which may lead to mural thrombus formation and considerable morbidity and mortality. There may also be associated angioedema or urticaria. Treatment is with high-dose corticosteroids (e.g. prednisolone 50 mg, which leads to a response in around 50% of cases). Steroid-sparing agents such as cyclophosphamide or azathioprine may also be of some value. In those patients who carry the FIP1L1/PDGFRA mutation, imatinib is the drug of choice.

A Churg-Strauss syndrome

30–40% of patients with Churg–Strauss are positive for pANCA, and they have symptoms of asthma rather than merely the chronic cough seen here. Other features include mononeuritis multiplex, GI bleeds and glomerulonephritis, which aren't seen here.

C	Acute eosinophilic pneumonia

Acute eosinophilic pneumonia has a much more rapid onset of symptoms, with significant evidence of respiratory failure within 7 days to 1 month from when features first appear.

D	Chronic pulmonary eosinophilia

The extra-pulmonary features seen here are inconsistent versus a diagnosis of chronic pulmonary eosinophilia. Hence this is much less likely to be the underlying diagnosis.

E	Chronic parasitic infection

A 65-year-old woman, known to have stable rheumatoid arthritis for 20 years, has been re-referred to the Rheumatology Clinic with symptoms of chronic foul-smelling diarrhoea. She says she has lost 10 kg in weight in last 6 months. Her general appetite is quite poor as well. She finds herself quite lethargic and has noticed peripheral oedema early in the mornings. According to her, her joints have not troubled her for a long time. She is currently on methotrexate and folic acid.

On examination, she has waxy skin, with plaques clustered in the axillary folds, and multiple bruises are seen. No lymph nodes are palpable. Joint examination showed no evidence of synovitis. Her pulse rate is 80 bpm, blood pressure (BP) 140/90 mmHg and respiratory rate (RR) 16 breaths/min. Heart sounds are normal, and she has good air entry bilaterally, with no added sounds. Abdominal examination reveals hepatosplenomegaly. There is no ascites, and no other masses are felt.

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hepatosplenomegaly. There is no ascites, and no other masses are felt. Central nervous system examination shows evidence of peripheral neuropathy.

Investigations:

Sodium (Na^+)	143 mmol/l
Potassium (K^+)	4.5 mmol/l
Urea	7.8 mmol/l
Creatinine (Cr)	120 µmol/l
Liver function tests	Normal
Thyroid function tests	Normal
C-reactive protein (CRP)	20 mg/l
Erythrocyte sedimentation rate (ESR)	9 mm/first hour
24-h urinary analysis	Shows 5 g of proteinuria

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Chest X-ray	Shows an enlarged cardiac silhouette
Electrocardiogram (ECG)	Shows low-voltage QRS complexes

Which one of the following will be of most diagnostic value?

A	Bone marrow aspirate and biopsy
B	Serial sputum samples for acid-fast bacilli and tuberculosis (TB) culture
C	Rectal biopsy
D	Nerve conduction studies
E	Faecal elastase

33301

C Rectal biopsy

This patient has many of the hallmarks of systemic amyloidosis. An abdominal fat biopsy or a rectal biopsy is the best way to make the diagnosis. A positive Congo red histological stain helps to establish diagnosis. The AA type of amyloid is seen secondary to a host of chronic inflammatory conditions, including long-standing rheumatoid arthritis, tuberculosis, bronchiectasis, familial Mediterranean fever, and leprosy. Amyloidosis should be suspected in any patient with an underlying chronic inflammatory disease who develops hepatosplenomegaly, malabsorption, cardiac disease or proteinuria. Cardiac disease usually consists of congestive heart failure with low QRS-complex voltage and exquisite sensitivity to digitalis.

Echocardiography shows a characteristic speckled appearance and may also be helpful in contributing to the diagnostic process. Waxy

to the diagnostic process. Waxy papules in the axillary folds may signal the deposition of amyloid in the skin; purpura after minor skin trauma is not uncommon. In addition to amyloid-induced synovitis, peripheral neuropathy and carpal tunnel syndrome may be seen.

A	Bone marrow aspirate and biopsy

Bone marrow aspirate may reveal amyloid deposits, but it is significantly more invasive, when compared to a rectal biopsy, and is therefore not the preferred option.

B	Serial sputum samples for acid-fast bacilli and tuberculosis (TB) culture

Given respiratory examination is normal and there are no symptoms of cough, TB is unlikely as the cause of her current symptoms.

A 40-year-old man presents with breathlessness of 3 months' duration. He is now moderately breathless on climbing a single flight of stairs. He had been working as a gym instructor before the onset of symptoms.

He first noticed his symptoms after a heavy bout of 'indigestion' that occurred on the day of a close relative's funeral. He was treated with chemotherapy and mediastinal radiotherapy for Hodgkin's disease 10 years previously and has been in complete remission ever since, although he says his chest X-ray remains abnormal.

His chest X-ray shows a widened mediastinum and borderline cardiomegaly, and an electrocardiogram (ECG) shows poor R-wave progression in the anterior chest leads with Q waves in V2, 3 and 4. On examination he has a few crackles throughout the chest, most prominent at the bases and an audible third heart sound. He has prominent neck veins.

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R-wave progression in the anterior chest leads with Q waves in V2, 3 and 4. On examination he has a few crackles throughout the chest, most prominent at the bases and an audible third heart sound. He has prominent neck veins.

What is the most likely diagnosis?

A Cardiac amyloid infiltration

B Cardiac failure secondary to previous anthracycline administration

C Heart failure secondary to anterior myocardial infarction

D Pericardial effusion from progressive Hodgkin's disease

E Progressive pulmonary fibrosis from bleomycin

71093

2:38

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C	Heart failure secondary to anterior myocardial infarction

This man has developed heart failure which was associated with chest pain, the ‘heavy bout of indigestion’, with a characteristic ECG diagnostic of an infarct more than a few days previously. He is at high risk of coronary artery disease given his previous radiotherapy to the mediastinum.

B	Cardiac failure secondary to previous anthracycline administration

Anthracycline cardiomyopathy would not explain the sudden change in symptoms, but it can occur late after chemotherapy – classically with doses exceeding 450 mg/m^2.

A	Cardiac amyloid infiltration

Amyloid can occur with myeloma but is not seen with Hodgkin’s disease.

Question 18 of 139

chemotherapy - classically with doses exceeding 450 mg/m^2.

A	Cardiac amyloid infiltration

Amyloid can occur with myeloma but is not seen with Hodgkin’s disease.

D	Pericardial effusion from progressive Hodgkin’s disease

Progressive Hodgkin’s disease is unlikely but not impossible at 10 years - persistent masses are common after treatment in Hodgkin’s patients.

E	Progressive pulmonary fibrosis from bleomycin

Pulmonary fibrosis secondary to bleomycin would not explain the cardiac changes or the sudden change in symptoms.

71093

Rate this question: ⊖ ☆☆☆☆☆

A 56-year-old woman has been referred to clinic. She has had two episodes of shingles in the past 2 months and her GP had noticed persisting lymphadenopathy. The patient currently feels well and there is no past history of note.

Examination reveals some petechiae on her back, cervical lymphadenopathy and mild splenomegaly.

Investigations:

Hb	8.9 g/dl
WBC	48 x 10^9/l (lymphocytes 40 x 10^9/l)
PLT	116 x 10^9/l
Blood film	Smear cells

What is the most likely diagnosis?

A Hairy cell leukaemia

B Acute lymphoblastic

2:40

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WBC	48 x 10⁹/l (lymphocytes 40 x 10⁹/l)
PLT	116 x 10⁹/l
Blood film	Smear cells

What is the most likely diagnosis?

A Hairy cell leukaemia

B Acute lymphoblastic leukaemia

C Splenic lymphoma

D Non-Hodgkin’s lymphoma

E Chronic lymphocytic leukaemia

7080

Submit

months and her GP had noticed persisting lymphadenopathy. The patient currently feels well and there is no past history of note.

Examination reveals some petechiae on her back, cervical lymphadenopathy and mild splenomegaly.

Investigations:

Hb	8.9 g/dl
WBC	48 x 10^9/l (lymphocytes 40 x 10^9/l)
PLT	116 x 10^9/l
Blood film	Smear cells

What is the most likely diagnosis?

Your answer was correct

A Hairy cell leukaemia

B Acute lymphoblastic leukaemia

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E Chronic lymphocytic leukaemia

CLL is the most common adult leukaemia in the Western world. The diagnosis can be discovered incidentally, or patients can have symptoms of anaemia, recurrent bleeding and recurrent infections. Examination can reveal lymphadenopathy with hepatosplenomegaly. A full blood count will show a raised WBC with a lymphocytosis. The blood film will show smudge cells, as these are more friable. Immunophenotyping will confirm the diagnosis, with CD19 and CD5 white cell markers likely to be present.

A Hairy cell leukaemia

Hairy cell leukaemia is usually associated with a low white blood cell count rather than the mature lymphocytosis seen here.

B	Acute lymphoblastic leukaemia

ALL is unlikely to be the diagnosis given that blast cells have not been found to be present on the blood film.

C	Splenic lymphoma

Primary splenic lymphoma is associated with enlargement of the spleen as is seen here, but is not associated with the marked elevation in white blood cell count.

D	Non-Hodgkin’s lymphoma

Non-Hodgkin’s lymphoma is associated with peripheral lymphadenopathy and impaired immune function, although the marked elevation in peripheral blood lymphocyte count is not seen.

7080

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A 56-year-old woman presents with headaches and malaise. She is hypertensive and has a past medical history of deep venous thrombosis (DVT) following a long-haul trip on an airliner. She is a non-smoker.

The examination is unremarkable apart from the fact she is obese, with a BMI of 31. Blood gases were normal.

Investigations:

Urate	0.53 mmol/l (0.19–0.36)
Hb	19.0 g/dl
WCC	15.0 x 10^9/l
PLT	450 x 10^9/l
Erythropoietin	1 mU/ml (0–19)

What is the most likely diagnosis?

A	Polycythaemia rubra vera
B	Chronic myelocytic leukaemia

Question 20 of 139

Urate	0.53 mmol/l (0.19–0.36)
Hb	19.0 g/dl
WCC	15.0 x 10^9/l
PLT	450 x 10^9/l
Erythropoietin	1 mU/ml (0–19)

What is the most likely diagnosis?

A	Polycythaemia rubra vera
B	Chronic myelocytic leukaemia
C	Essential thrombocythaemia
D	Obstructive sleep apnoea
E	Renal cell carcinoma

9844

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of 31. Blood gases were normal.

Investigations:

Urate	0.53 mmol/l (0.19–0.36)
Hb	19.0 g/dl
WCC	15.0 x 10^9/l
PLT	450 x 10^9/l
Erythropoietin	1 mU/ml (0–19)

What is the most likely diagnosis?

Your answer was correct

A Polycythaemia rubra vera

B Chronic myelocytic leukaemia

C Essential thrombocythaemia

D Obstructive sleep apnoea

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A Polycythaemia rubra vera

The results are the picture of polycythaemia due to increase in red blood cells (absolute polycythaemia) or decrease in the plasma volume (relative polycythaemia).

Polycythaemia rubra vera (PRV) is a malignant disorder of stem cells (i.e. they display abnormal responses to growth factors) characterised by over-proliferation in the bone marrow of erythroid, myeloid and megakaryocytic elements. It has an incidence of 5–17/million population/year. Patients may present with venous thromboses at unusual sites (e.g. portal vein, hepatic vein). Neurological manifestations are also common (transitory ischemic attack (TIAs), cardiovascular accident (CVAs), fluctuating dementia), as is joint pain and gout.

Bone marrow examination shows hypercellularity with clustered mature megakaryocytes and the formation of erythroid colonies without exogenous

4:45

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B Chronic myelocytic leukaemia

CML is a myeloproliferative disorder with predominant elevation in white cells. The marked elevation in haemoglobin makes this less likely as the underlying diagnosis. In CML a greater increase in cells from the myelocytic line, including for example basophils, would be expected.

C Essential thrombocythaemia

In essential thrombocythaemia, it is usually only the platelets that are elevated.

D Obstructive sleep apnoea

Secondary polycythaemia due to chronic hypoxia causes erythropoietin release in chronic obstructive pulmonary disease (COPD), Eisenmenger syndrome and OSA.

E Renal cell carcinoma

A 32-year-old woman presents with dizziness. Symptoms have been coming on for the last few months, and she now needs help with standing. She is treated with bendroflumethiazide for recently diagnosed hypertension, smokes 10 cigarettes daily and drinks around 30 units per week of alcohol. She is one of four children, a brother having died in the past of renal cancer.

On direct questioning, she admits to cough productive of phlegm, present most mornings for the last few years, but has normal exercise tolerance.

On examination, she is noticeably plethoric. There is an audible expiratory wheeze throughout the chest. Oxygen saturations are normal. There is nystagmus present looking left or right. Fundoscopy reveals dilated retinal veins. She has a broad-based gait, and is unsteady with eyes open or closed.

Investigations:

Hb	20.3 g/dl
WCC	7.1×10^9/l

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Hb	20.3 g/dl
WCC	7.1 x 10^9/l
Platelets	169 x 10^9/l
Haematocrit	0.61
Red cell mass	2312 ml (1312–2187)
Plasma volume	2392 ml (2362–3938)
Erythroid culture in the absence of erythropoeitin	No endogenous erythroid colony formation

Which of the following is the most likely diagnosis?

A Primary polycythaemia rubra vera

B Von Hippel–Lindau syndrome

C Renal cell carcinoma with endogenous erythropoietin production

Question 21 of 139

Erythroid culture in the absence of erythropoeitin	No endogenous erythroid colony formation

Which of the following is the most likely diagnosis?

A Primary polycythaemia rubra vera

B Von Hippel–Lindau syndrome

C Renal cell carcinoma with endogenous erythropoietin production

D Gaisbock syndrome

E Alcohol abuse

7538

She is one of four children, a brother having died in the past of renal cancer.

On direct questioning, she admits to cough productive of phlegm, present most mornings for the last few years, but has normal exercise tolerance.

On examination, she is noticeably plethoric. There is an audible expiratory wheeze throughout the chest. Oxygen saturations are normal. There is nystagmus present looking left or right. Fundoscopy reveals dilated retinal veins. She has a broad-based gait, and is unsteady with eyes open or closed.

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Haematocrit	0.61
Red cell mass	2312 ml (1312–2187)
Plasma volume	2392 ml (2362–

Question 21 of 139

B Von Hippel-Lindau syndrome

This patient has a high haematocrit; with an increased red cell mass and a low-normal plasma volume, confirming true polycythaemia. Von Hippel-Lindau (VHL) syndrome is an autosomal dominant condition that leads to retinal and central nervous system tumours, as well as phaeochromocytomas. Signs of VHL syndrome include balance disturbance, hypertension, headaches and dizziness. Death is often due to renal cell carcinoma.

Criteria are the following:

- More than one hemangioblastoma in the CNS (brain, spinal cord) or eye.
- A single hemangioblastoma in the CNS or retina, plus a visceral manifestation (multiple renal, pancreatic or hepatic cysts; pheochromocytoma; renal cancer).

- Positive family history plus any one of the above clinical manifestations.
- Elucidation of a deleterious mutation in the *VHL* gene.

Management depends on the site of individual tumours, but close ophthalmic, renal and radiographical follow-up is recommended for all patients. There is no ultimate cure for VHL. A proportion of cerebellar haemangiomas secrete erythropoietin-like substances, leading to a secondary polycythaemia.

Erythroid colony studies suggest that her red cells do not show autonomous growth; autonomous growth of erythroid colonies is taken as a sign of primary polycythaemia, where erythropoiesis has escaped the control of erythropoietin; erythroid colony studies are thought to have high specificity for detecting primary versus secondary polycythaemia, but the technique is poorly standardized so remains an experimental tool.

This is caused by bone marrow overproduction of red blood cells (and sometimes white cells and platelets). Patients maybe asymptomatic, presenting with blood clots, itching and skin changes.

C Renal cell carcinoma with endogenous erythropoietin production

Rare cases of renal cell carcinoma proliferate with endogenous erythropoietin production. There was no endogenous erythroid colony found on testing.

D Gaisbock syndrome

This is a form of pseudo-polycythaemia, usually found in obese men with hypertension causing a reduction in plasma volume.

E Alcohol abuse

It is not uncommon to see borderline

erythropoietin production. There was no endogenous erythroid colony found on testing.

D	Gaisbock syndrome

This is a form of pseudo-polycythaemia, usually found in obese men with hypertension causing a reduction in plasma volume.

E	Alcohol abuse

It is not uncommon to see borderline plasma volumes in patients with excessive alcohol intake (or on diuretics).

An 18-year-old girl presents with sudden-onset dysarthria and right-sided weakness. You see her 12 h after the event and her symptoms have now resolved. She takes the oral contraceptive pill. She is in full-time education and smokes 5–10 cigarettes daily. Alcohol intake is minimal. She lives with her parents. Family history is unremarkable other than a possible deep vein thrombosis in an aunt.

Examination is unremarkable, other than a lacy rash over her thighs and a grade II ejection systolic murmur. Computed tomography of the brain performed 2 h after admission is unremarkable.

Investigations:

Hb	12.3 g/dl
WCC	3.5 x 10^9/l
PLT	135 x 10^9/l
APTT	45 s (30–40)

What is the most likely identity of the rash?

Hb	12.3 g/dl
WCC	3.5 x 10⁹/l
PLT	135 x 10⁹/l
APTT	45 s (30–40)

What is the most likely identity of the rash?

A Erythaema ab igne

B Erythaema chronicum migrans

C Livedo reticularis

D Erythroderma

E Erythaema multiforme

6378

education and smokes 5–10 cigarettes daily. Alcohol intake is minimal. She lives with her parents. Family history is unremarkable other than a possible deep vein thrombosis in an aunt.

Examination is unremarkable, other than a lacy rash over her thighs and a grade II ejection systolic murmur. Computed tomography of the brain performed 2 h after admission is unremarkable.

Investigations:

Hb	12.3 g/dl
WCC	3.5 x 10^9/l
PLT	135 x 10^9/l
APTT	45 s (30–40)

What is the most likely identity of the rash?

Your answer was correct

A	Erythaema ab igne

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C Livedo reticularis

This is a case of a young woman with anti-phospholipid syndrome, also known as Hughes syndrome. This is diagnosed in patients with characteristic clinical phenomena (venous and arterial thromboembolism, recurrent first trimester miscarriages, livedo reticularis, chorea and Libman–Sacks endocarditis) in whom positive anti-cardiolipin antibodies or a lupus anticoagulant are detected on two separate occasions, separated by at least 6 weeks.

The condition is managed by lifelong anticoagulation with warfarin, at a target international normalised ratio (INR) of 2–3 (higher targets were previously used, but a randomised controlled double-blind trial (Crowther et al, *New England Journal of Medicine*, 2003) did not support any greater therapeutic effect of high intensity anticoagulation. The paradoxical prolongation of the activated partial

prolongation of the activated partial thromboplastin time is due to antibodies to phospholipids, which is critical to the functioning of the assay. However, a normal APTT does not rule out the presence of a lupus anticoagulant; to rule this out you need to assess phospholipid-dependent measures of clotting, such as the dilute Russell viper venom time.

A	Erythaema ab igne

Erythema ab igne is associated with reticulated erythema, hyperpigmentation, skin scaling and telangiectasia over the area which has been subject to local heat.

B	Erythaema chronicum migrans

Erythema chronicum migrans is a rash characteristic of Lyme disease, which extends out from the original tick bite or eschar.

Question 23 of 139

A 70-year-old woman presents with fatigue and confusion that has come on gradually over several weeks. She is a retired secondary school teacher who was still tutoring on a part-time basis until 3 months ago but has recently become reliant on family and neighbours for basic self-care. She has no previous medical history of note and is taking only antacids for occasional dyspepsia.

On examination, she is obese, with a blood pressure of 175/100 mmHg. She is disorientated; tone, power and reflexes are all within normal limits. Plantar responses are downgoing. Fundoscopy shows prominent retinal veins, but is otherwise normal. There are bi-basal crackles at both bases.

Blood tests are shown below:

		Normal values
Haemoglobin (Hb)	9.5 g/dl	
White cell count (WCC)	5.3 × 10^9/l	

5:37

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Haemoglobin (Hb)	9.5 g/dl	
White cell count (WCC)	5.3 × 10^9/l	
Platelets (PLT)	120 × 10^9/l	
Urea	10.3 mmol/l	2.5–7.5
Bilirubin	21 µmol/l	1–22
Albumin	29 g/l	37–49
Protein	113 g/l	60–76
Erythrocyte sedimentation rate (ESR)	95 mm/first hour	
Calcium	2.3 mmol/l	2.2–2.6

What test is most likely to help establish the cause of confusion?

A Bone scan

5:38

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Erythrocyte sedimentation rate (ESR)	95 mm/first hour	
Calcium	2.3 mmol/l	2.2-2.6

What test is most likely to help establish the cause of confusion?

A	Bone scan
B	Urine for Bence Jones protein
C	Serum protein electrophoresis
D	Skeletal survey
E	Magnetic resonance imaging (MRI) brain

33294

Submit

C Serum protein electrophoresis

The question asks for the test most likely to confirm the cause of the confusion. Myeloma or Waldenström's macroglobulinaemia leading to clinically significant hyperviscosity are the most likely cause here. Serum immunoglobulins do not confirm the presence of a paraprotein, whereas serum protein electrophoresis will. This is because a number of inflammatory conditions may result in a global increase in immunoglobulins.

If a paraprotein is found, a bone marrow trephine can help make a tissue diagnosis of an associated myeloma [in the case of immunoglobulin G (IgG)/immunoglobulin A (IgA) paraproteins] or lymphoplasmacytoid lymphoma [in the case of immunoglobulin M (IgM) paraprotein] and help to differentiate between Waldenström's macroglobulinaemia and myeloma, but this test will not directly help explain the patient's confusion. Great care should be

confusion. Great care should be exercised before patients with hyperviscosity are transfused, as any further increase in viscosity may precipitate a cerebral event. Treatment is with chemotherapy targeted to the underlying condition and, where transfusion is urgently required, plasmapheresis first.

A Bone scan

Bone scanning is of value in multiple myeloma, but of no utility in Waldenström's macroglobulinaemia due to only very rare reports of skeletal system involvement.

B Urine for Bence Jones protein

Although urine for Bence Jones protein should certainly be performed in all suspected myelomas, it is extremely rare for light chain disease to cause clinically apparent hyperviscosity. This is because viscosity is directly proportional to the size of the molecule causing it:

extremely rare for light chain disease to cause clinically apparent hyperviscosity. This is because viscosity is directly proportional to the size of the molecule causing it; therefore, IgM, which is pentameric, is most likely to cause hyperviscosity, followed by the dimeric IgA, then IgG.

D	Skeletal survey

The skeleton is usually not involved in Waldenström's macroglobulinaemia, meaning that a skeletal survey is not usually considered of value in the workup of the condition.

E	Magnetic resonance imaging (MRI) brain

MRI brain may show periventricular white matter changes, but it is not helpful in differentiating whether these are due to microvascular disease or due to an underlying hyperviscosity syndrome.

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A 23-year-old woman presents with a swollen, tender left calf having returned from Australia on a long-haul flight. She takes the oral contraceptive pill, but is a non-smoker and has no other significant risk factors.

On examination, her blood pressure and pulse are normal and her chest is clear. Her left leg is swollen and tender, and the calf is significantly larger than the right. D-dimers are slightly elevated at 420. An initial ultrasound is negative.

Which of the following is the next step?

A Start low-molecular weight heparin

B Repeat ultrasound in 7 days

C Reassure

D Start warfarin

On examination, her blood pressure and pulse are normal and her chest is clear. Her left leg is swollen and tender, and the calf is significantly larger than the right. D-dimers are slightly elevated at 420. An initial ultrasound is negative.

Which of the following is the next step?

Your answer was correct

A Start low-molecular weight heparin

B Repeat ultrasound in 7 days

C Reassure

D Start warfarin

E Start rivaroxaban

Explanation

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B	Repeat ultrasound in 7 days

In the presence of a definitive investigation result, even though the d-dimer is positive and clinical suspicion of DVT is high, according to SIGN guidelines this patient shouldn't be anticoagulated, but instead should be re-scanned, either with an ultrasound or a venogram 7 days after the initial event. It is of course possible that she has suffered a calf muscle tear leading to the elevated d-dimers and symptom presentation seen here.

A	Start low-molecular weight heparin

Given an initial normal ultrasound scan and a slightly elevated D-dimer at only 420, there is no indication to begin low molecular weight heparin. It may indeed cause an increased risk of bleeding with little immediate obvious benefit.

C	Reassure

C Reassure

The clinical suspicion for a DVT is high, and therefore the patient should be advised to attend for a repeat scan 7 days later.

D Start warfarin

According to SIGN guidelines, the patient should be re-scanned in 7 days and not anticoagulated. Warfarin is the preferred anticoagulant for patients in whom factor Xa or direct thrombin inhibitors are not available, and for patients with severe renal insufficiency. Warfarin requires multiple visits for INR monitoring and has a higher bleeding risk when compared to direct oral anticoagulants; however, antidotes for warfarin-related bleeding are more readily available. Thus, it may also be preferred in those with a preference or requirement for a readily reversible antidote (e.g. need for frequent interventions) and those for whom therapeutic anticoagulation needs to be monitored (e.g. poor compliance).

therapeutic anticoagulation needs to be monitored (e.g. poor compliance).

E Start rivaroxaban

According to SIGN guidelines, the patient should be re-scanned in 7 days and not anticoagulated. Factor Xa inhibitors (e.g. rivaroxaban, apixaban, edoxaban) and oral direct thrombin inhibitors (dabigatran) are preferred anticoagulants for most hemodynamically stable, non-pregnant patients who do not have severe renal insufficiency or active cancer. While rivaroxaban and apixaban can be administered as monotherapy, edoxaban and dabigatran are preferably administered following a 5-day course of heparin (ie as dual therapy – low-molecular weight or unfractionated heparin).

A 19-year-old woman is referred from her GP complaining of menorrhagia and easy bruising. Her older sister also has menorrhagia and frequent nose bleeds.

A summary given by her GP of tests already performed shows:

PT	13 s (10–14)
aPTT	50 s (30–45)
PLT	263 × 10^9/l (150–400)
INR	0.9 (0.0–1.2)
Hb	10.5 g/dl (11.5–16.0)
Ristocetin co-factor (RoCF)	24 IU/dl (50–200)
Group & save blood type	A-positive
Activated protein C resistance ratio	2.4 (>2.1)

What diagnosis would best fit this

Ristocetin co-factor (RoCF)	24 IU/dl (50–200)
Group & save blood type	A-positive
Activated protein C resistance ratio	2.4 (>2.1)

What diagnosis would best fit this clinical picture?

A Haemophilia A

B Factor V deficiency

C Christmas disease

D Antiphospholipid syndrome

E Von Willebrand's disease (vWD)

7642

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A summary given by her GP of tests already performed shows:

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Ristocetin co-factor (RoCF)	24 IU/dl (50–200)
Group & save blood type	A-positive
Activated protein C resistance ratio	2.4 (>2.1)

E Von Willebrand’s disease (vWD)

Von Willebrand’s disease is a common, inherited, genetically and clinically heterogeneous haemorrhagic disorder caused by a deficiency or dysfunction of the protein termed von Willebrand factor (vWF). This is a large, multimeric glycoprotein which functions as the carrier protein for factor VIII, by binding to and stabilizing this factor, and it also mediates the adhesion of platelets to sites of vascular injury.

The VWF gene is located near the tip of the short arm of chromosome 12. vWD is divided into three major categories:

(1) partial quantitative deficiency (type I),
(2) qualitative deficiency (type II), and
(3) total deficiency (type III).

Males and females are affected equally although the disease manifestations are more obvious in the female due to

are more obvious in the female due to menstruation and the associated menorrhagia.

The screening test used to diagnose the condition includes prothrombin time (PT), activated partial thromboplastin time (aPTT), factor VIII activity, vWF activity (ristocetin cofactor) and vWF antigen level determination. Ristocetin is an antibiotic that causes vWF to bind to and activate platelets. Platelets rapidly agglutinate in response to ristocetin, but the presence of plasma vWF is necessary for this reaction to occur. The PT is within the reference range, but the aPTT is mildly prolonged in half of these patients. The degree of platelet agglutination is proportional to the concentration of vWF in the plasma. This is called the vWF activity or ristocetin cofactor assay, and is variably reduced in patients with vWD.

A Haemophilia A

In this X-linked recessive condition, PT

In this X-linked recessive condition, PT is normal and APTT will either be severely prolonged in severe haemophilia A or normal/mildly prolonged in less severe case. It only occurs in males.

B	Factor V deficiency

This is a prothrombotic condition resulting from the mutation of factor V. There is a decreased activated protein C ratio with this condition.

C	Christmas disease

Also known as haemophilia , this is a genetic mutation of factor IX and would show normal levels of von Willebrand's factor, normal PT and normal or slightly prolonged APTT. There would be very low or absent levels of factor IX. It also is X-linked and occurs in males.

D	Antiphospholipid syndrome

C	Christmas disease

Also known as haemophilia , this is a genetic mutation of factor IX and would show normal levels of von Willebrand's factor, normal PT and normal or slightly prolonged APTT. There would be very low or absent levels of factor IX. It also is X-linked and occurs in males.

D	Antiphospholipid syndrome

This is a prothrombotic condition and is diagnosed by lupus anticoagulant present on two tests more than 12 weeks apart, anticardiolipin antibody presence, and the presence of anti-2-beta-glycoprotein I. APTT maybe prolonged due to positive lupus anticoagulant.

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A 32-year-old woman who has suffered a bleed post-caesarean section receives the second unit of a 3-unit blood transfusion and develops sudden onset shortness of breath, fever and cough. There is no history of flank pain. The unit is immediately stopped.

On examination, she looks unwell; her BP is 100/62 mmHg, with a pulse of 95/min. Auscultation of the chest reveals bilateral crackles consistent with pulmonary oedema.

Investigations:

Hb	9.6 g/dl
WCC	3.9 x 10^9/l
PLT	130 x 10^9/l
Na^+	139 mmol/l
K^+	4.9 mmol/l
Urea	8.1 mmol/l
Creatinine	110 µmol/l

Which of the following is the most

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Na⁺	139 mmol/l
K⁺	4.9 mmol/l
Urea	8.1 mmol/l
Creatinine	110 µmol/l

Which of the following is the most likely diagnosis?

A ABO incompatability

B Rhesus incompatability

C Transfusion Associated Lung Injury

D Circulatory overload

E Anaphylaxis

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C Transfusion Associated Lung Injury

In all likelihood this is non-cardiogenic pulmonary oedema, as evidenced by the chest signs. The lack of an elevated JVP and the low normal blood pressure count against a diagnosis of fluid overload. This fits best with a diagnosis of TRALI.

Two hypotheses exist as to the cause of TRALI: (1) anti-HLA antibodies are transfused into the patient, leading to neutrophil activation, release of cytokines and pulmonary oedema; and (2) neutrophils ready primed by surgery or infection react with bioactive substances in the transfused blood, leading to similar neutrophil activation. Non-cardiogenic pulmonary oedema can be differentiated from fluid overload by measurement of BNP if there is an element of diagnostic confusion. Diuretics are not beneficial in the management of the condition, and she should be managed with supportive care, including transfer to ITU for consideration of intubation and

ITU for consideration of intubation and ventilation if required. The mortality of TRALI is estimated at 5–13% depending on case series.

A	ABO incompatability

ABO incompatibility leads to acute haemolysis with a severe transfusion reaction, associated with mortality of up to 10%. Symptoms are similar to anaphylaxis, although the reaction is not mediated by IgE.

B	Rhesus incompatability

Non-ABO incompatibility reactions – for example, those associated with rhesus incompatibility, are less severe than ABO incompatibility, although significant haemolysis is still seen.

D	Circulatory overload

Given that this patient is a 32-year-old woman, circulatory overload in

D Circulatory overload

Given that this patient is a 32-year-old woman, circulatory overload in response to a blood transfusion is extremely unlikely. The low blood pressure would also not fit well with circulatory overload.

E Anaphylaxis

Bacterial contamination of units of red cells is thankfully extremely rare but, where it occurs, circulatory collapse with hypotension and rigors is seen early on in the transfusion process.

20949

A 50-year-old man with myelodysplasia complains of breathlessness on exertion. He was diagnosed with myelodysplasia 3 years ago and since then has been on 2 units of blood every 3 weeks to maintain his haemoglobin above 10 g/dl. He has noticed over the last 3 months increasing exertional breathlessness despite maintaining his haemoglobin above 10.

Examination shows a slim man with a greyish skin colour. Pulse 90 beats per minute (bpm), sinus rhythm. Heart sounds are normal. Jugular venous pressure is not raised. Cardiac apex is palpable at the anterior axillary line. There are bilateral basal crackles on auscultation of the chest, abdominal examination is normal.

Investigations:

Hb	11.3 g/dl
WCC	1.3 x 10^9/l
PLT	23 x 10^9/l
Neutrophils	0.3 x 10^9/l

Glucose	12.4 mmol/l (3.0-6.0)

What is the most appropriate intervention?

A	Increase the transfusion program to maintain haemoglobin above 12 g/dl
B	Commence subcutaneous recombinant erythropoietin to raise the haemoglobin to 12 g/dl
C	Start venesection program to reduce ferritin to less than 1000
D	Commence iron chelation with subcutaneous desferrioxamine
E	Commence hydroxyurea or similar cytotoxic to treat myelodysplasia

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D Commence iron chelation with subcutaneous desferrioxamine

This patient has early signs of iron overload secondary to chronic blood transfusion – grey skin, early heart failure and diabetes. There are limited options for intervention, and given the transfusion needs of this patient with iron overload, desferrioxamine is the most appropriate choice. It needs to be given for 8-12 h per day for 5-7 days per week and is thus a major undertaking for the patient. Side effects of therapy are common and include high-frequency deafness and retinopathy.

E Commence hydroxyurea or similar cytotoxic to treat myelodysplasia

Hydroxyurea won’t reduce transfusion requirements or iron overload in the short term, and thus intervention with an iron chelator is the preferred choice

haemoglobin above 12 g/dl

This runs the risk of further worsening iron overload and won't improve symptoms of cardiac failure.

B	Commence subcutaneous recombinant erythropoietin to raise the haemoglobin to 12 g/dl

Commencing erythropoietin to reduce the transfusion requirement is an attractive option, but is only likely to work in patients with low transfusion requirements (<1 unit per month) and does not address the underlying problem of iron overload.

C	Start venesection program to reduce ferritin to less than 1000

Although this would impact on iron overload, it would worsen anaemia and defeat the object of regular transfusions.

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A 42-year-old man is admitted with headaches and visual disturbance. The patient is known to have Waldenström's macroglobulinaemia. While in the Assessment Unit, he has a nosebleed that is continuing to ooze and is difficult to control.

Fundoscopy shows dilated retinal veins with retinal haemorrhage in the right eye. He has pale conjunctivae and appears breathless.

Observations:

Blood pressure	115/65 mmHg
Heart rate	120 bpm
Temperature	37 °C

The on-call ear, nose and throat (ENT) surgeon is called to pack his nose.

What is the best acute treatment for his hyperviscosity?

A Cyclophosphamide

B Plasmapheresis

Question 28 of 139

Blood pressure	115/65 mmHg
Heart rate	120 bpm
Temperature	37 °C

The on-call ear, nose and throat (ENT) surgeon is called to pack his nose.

What is the best acute treatment for his hyperviscosity?

A Cyclophosphamide

B Plasmapheresis

C Haemoperfusion

D Intravenous (IV) fresh frozen plasma (FFP)

E IV methylprednisolone

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B Plasmapheresis

The patient is displaying signs and symptoms of hyperviscosity syndrome, most likely secondary to Waldenström's macroglobulinaemia. Patients present with bleeding, visual disturbances and neurological symptoms. Other conditions leading to hyperviscosity can include multiple myeloma, polycythaemia rubra vera and leukaemia. Initial treatment of choice is plasmapheresis, which can rapidly reduce the viscosity and the risk of thromboembolic events.

A Cyclophosphamide

Cyclophosphamide has a role in the primary treatment of Waldenström's macroglobulinaemia, but as part of combination therapy, usually with dexamethasone and rituximab. An acute presentation requires plasmapheresis.

C Haemoperfusion

C Haemoperfusion

Haemoperfusion is usually instigated to remove a toxic metabolite, with activated charcoal and resins both used as materials to pass blood over.

D Intravenous (IV) fresh frozen plasma (FFP)

Both FFP and albumin may be used to replace plasma removed in the plasmapheresis process, but case series suggest a better profile with respect to adverse events where albumin is replaced in place of FFP.

E IV methylprednisolone

Dexamethasone is the standard corticosteroid used in the treatment of Waldenström's macroglobulinaemia, in conjunction with rituximab and cyclophosphamide.

A 60-year-old Asian man presents to the Pre-clerking Clinic prior to his laparoscopic cholecystectomy for gallstones.

He has a history of hypertension, for which he takes ramipril 10 mg, but no other past medical history of note.

Investigations:

Hb	10.4 g/dl
WCC	4.5 × 10^9/l
PLT	195 × 10^9/l
Na^+	139 mmol/l
K^+	4.5 mmol/l
Creatinine	105 µmol/l
MCV	60 fl (80–96)
Ferritin	300 µmol/l (15–300)
Upper GI endoscopy	Normal

Which of the following is the most

	300)
Upper GI endoscopy	Normal

Which of the following is the most appropriate investigation to confirm the underlying cause of his anaemia?

A	Colonoscopy
B	Mesenteric angiography
C	Transferrin
D	Haemoglobin electrophoresis
E	Bone marrow aspirate

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D Haemoglobin electrophoresis

This man has asymptomatic microcytic anaemia and he is of Asian ethnic origin. His upper GI endoscopy is normal, as is his ferritin, which reduces the possibility of this being iron deficiency anaemia. The most likely cause is beta-thalassaemia trait, the diagnosis of which is best confirmed with haemoglobin electrophoresis. Patients with thalassaemia trait do not usually require any intervention. Bearing in mind that his ferritin of 300 is within the normal range, his anaemia will not be responsive to iron supplementation. Chelation therapy is only required in patients with thalassaemia major. Blood loss associated with laparoscopic cholescystectomy is likely to be relatively minor, and so blood transfusion would not be required prior to surgery.

A Colonoscopy

This would be the appropriate

This would be the appropriate investigation for iron deficiency anaemia after a normal gastroscopy.

B	Mesenteric angiography

This would be the investigation of choice in cases of unexplained blood loss or unidentifiable source (normal gastroscopy and colonoscopy), and in persistent iron deficiency anaemia.

C	Transferrin

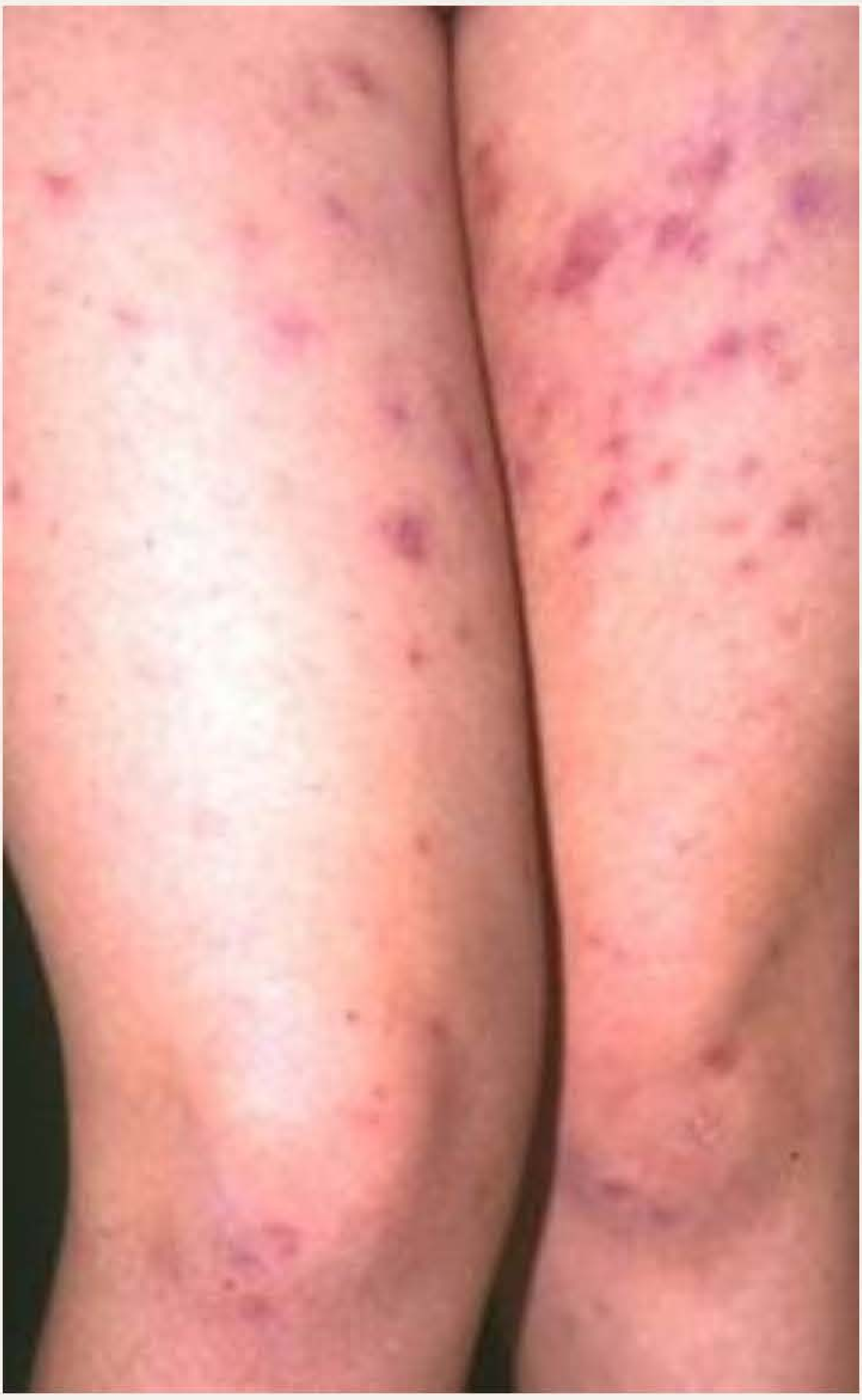
High transferrin levels are seen in iron deficiency anaemia, with subsequent decrease of the transferrin saturation and increase in TIBC (total iron-binding capacity).

E	Bone marrow aspirate

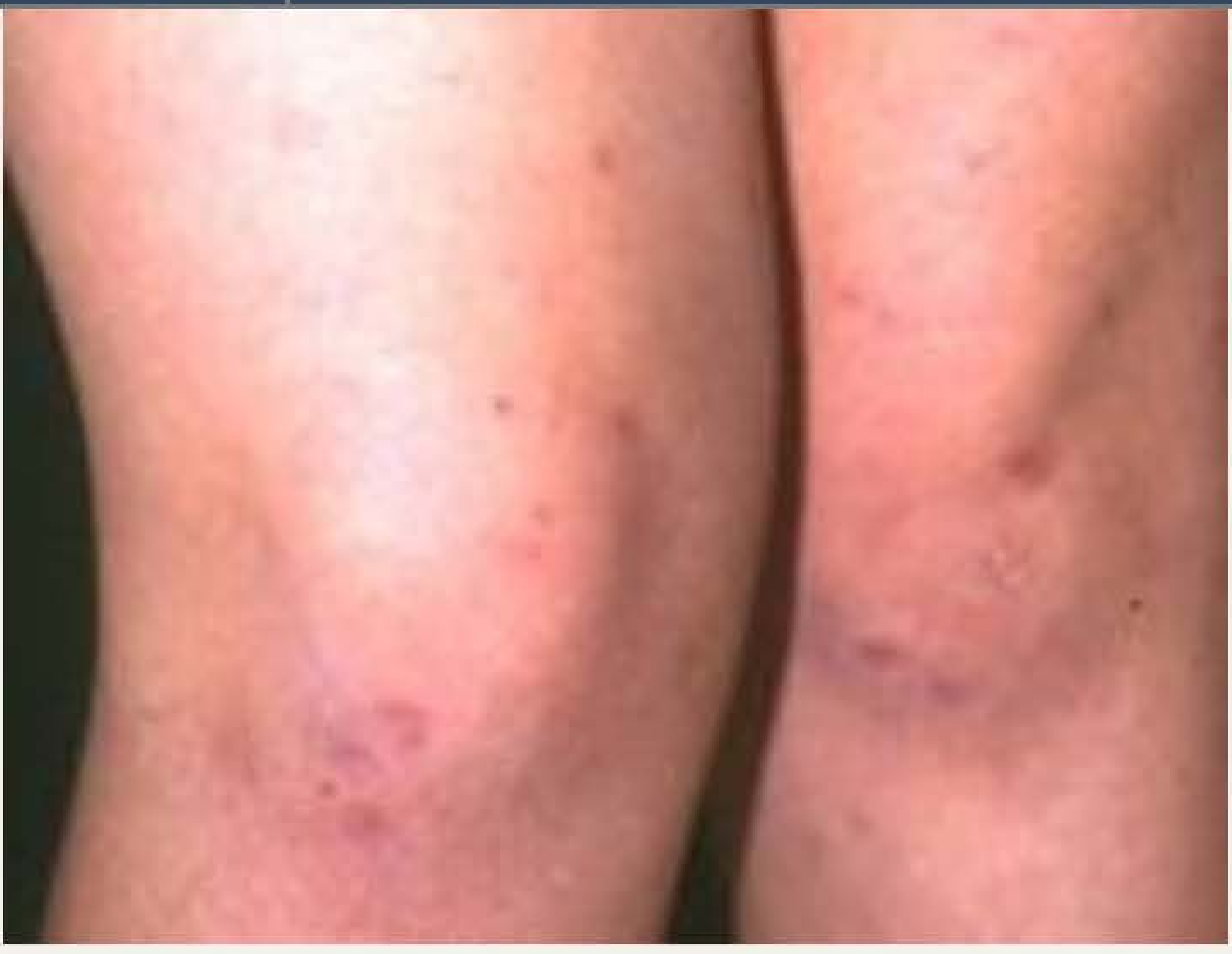
This is performed for the diagnosis of lympho- or myeloproliferative disorders.

A 30-year-old woman presents to her general practitioner with a 3-day history of cramping abdominal pain and vomiting.

A week previously, she had been absent from her job as a paint factory worker, with flu-like symptoms. She has now developed a rash (see image).



What complication might she be at most risk of developing?



What complication might she be at most risk of developing?

A	Epistaxis
B	Haemarthrosis
C	Pulmonary haemorrhage
D	Visual loss
E	Glomerulonephritis

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E Glomerulonephritis

The rash is that of Henoch–Schönlein purpura (HSP), an immunoglobulin A (IgA)-mediated small-vessel vasculitis characterised by purpura, arthritis, abdominal pain and haematuria. The cause is unknown; IgA-dominant immune complexes are present in smaller venules, capillaries and arterioles, representing a diffuse vasculitis that is secondary to hypersensitivity. HSP affects predominantly children (75% of cases occur between the ages of 2 and 11 years) and males are affected twice as commonly as females. However, adults can rarely be affected. Renal disease is the most common serious sequela (haematuria, proteinuria, nephritis, nephritic syndrome). Possible rarer complications include hepatosplenomegaly, myocardial infarction, pulmonary haemorrhage, pleural effusion, unnecessary abdominal surgery, intussusception, gastrointestinal bleeding, bowel infarction and nervous system vasculitic involvement.

HSP doesn't increase the risk of bleeding or cause a significant increase in blood pressure for the majority of cases, meaning that the risk of epistaxis is low.

B	Haemarthrosis

Joint haemorrhage is rarely seen in association with HSP, although polyarthritis is a common feature.

C	Pulmonary haemorrhage

Pulmonary haemorrhage is a more usual feature of Goodpasture syndrome and granulomatosis with polyangitis.

D	Visual loss

Episcleritis and episodes of central retinal artery occlusion are seen in HSP, although they are very much rarer than other manifestations such as glomerulonephritis and small-joint polyarthritis.

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A 65-year-old man is admitted with sudden-onset left upper limb and lower limb weakness. Apart from headaches, he was previously fit and well. He has never smoked and drinks two pints of beer a day.

Examination confirms left-sided motor and sensory deficit. He has an ejection systolic murmur at the right second intercostal space. His lungs sound clear, with good air entry. Abdominal examination reveals a mass in the left upper quadrant that is dull to percussion and moves downwards on inspiration.

Blood pressure is 157/89 mmHg, heart rate 70 bpm and regular, temperature 36.9 °C and oxygen saturation 92%.

Investigations:

Haemoglobin (Hb)	189 g/dl
White cell count (WCC)	12.2 × 10^9/l
Platelets (PLT)	462 × 10^9/l
Sodium (Na^+)	144 mmol/l

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Sodium (Na⁺)	144 mmol/l
Potassium (K⁺)	5.0 mmol/l
Urea	7.4 mmol/l
Creatinine	108 µmol/l
Hamatocrit	0.58
Leukocyte alkaline phosphatase (LAP) score	210 (reference 25-180)

What is the most likely diagnosis?

A Chronic myeloid leukaemia (CML)

B Primary polycythaemia (PP)

C Secondary polycythaemia

D Chuvash polycythaemia

E Renal cell carcinoma

Question 31 of 139

rate 70 bpm and regular, temperature 36.9 °C and oxygen saturation 92%.

Investigations:

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Creatinine	108 μmol/l
Hamatocrit	0.58
Leukocyte alkaline phosphatase (LAP) score	210 (reference 25-180)

What is the most likely diagnosis?

Your answer was incorrect

A Chronic myeloid leukaemia (CML)

B **Primary polycythaemia (PP)**

PP is a disorder resulting in an increase in the production of red blood cells (RBCs), WCCs and PLT. Patients can be asymptomatic but can also present with symptoms of headaches, tinnitus, visual disturbance and pruritus. Complications include arterial and venous thromboses, and patients with PP can present with Budd–Chiari syndrome. Other conditions associated with polycythaemia include gout, peptic ulceration and worsening of angina and intermittent claudication. Examination can reveal plethora, cyanosis, splenomegaly and hepatomegaly.

Investigations show increased Hb and haematocrit, with some patients also having increased WCC and PLT counts. Other tests can show elevated LAP scores, elevated vitamin B_{12}, normal/increased plasma volume, increased red cell mass and low erythropoietin levels. Treatment includes venesection, hydroxyurea and allopurinol. There is a risk for

erythropoietin levels. Treatment includes venesection, hydroxyurea and allopurinol. There is a risk for leukaemic transformation.

C **Secondary polycythaemia**

There is no evidence of chronic obstructive pulmonary disease (COPD) to suggest chronic hypoxia, and thus secondary polycythaemia. This would be a common explanation in patients with established chronic hypoxia.

A **Chronic myeloid leukaemia (CML)**

CML is more likely to be associated with anaemia and increased mature white cells (often an increase in basophils and eosinophils is seen), rather than the predominant increase in Hb featured here.

D **Chuvash polycythaemia**

Chuvash polycythaemia is congenital

CML is more likely to be associated with anaemia and increased mature white cells (often an increase in basophils and eosinophils is seen), rather than the predominant increase in Hb featured here.

D Chuvash polycythaemia

Chuvash polycythaemia is congenital erythrocytosis, which is inherited in an autosomal recessive fashion and is prominent in the autonomous Russian Republic of Chuvashia.

E Renal cell carcinoma

The absence of a renal mass and the elevated LAP score favours a haematological malignancy, rather than renal cell carcinoma here.

7066

Question 32 of 139

A 64-year-old man presents with a first spontaneous haematoma in his right thigh. Past medical history of note includes rheumatoid arthritis, for which he takes sulphasalazine and low-dose prednisolone.

Investigations:

Hb	11.9 g/dl
WCC	6.1 × 10^9/l
PLT	201 × 10^9/l
Na^+	140 mmol/l
K^+	4.4 mmol/l
Creatinine	100 µmol/l
PT	15s (11.5-15.5)
APTT	41s (30-40)
Lupus anti-coagulant	-

Which of the following is the most likely diagnosis?

A Haemophilia A

Creatinine	100 µmol/l
PT	15s (11.5-15.5)
APTT	41s (30-40)
Lupus anti-coagulant	-

Which of the following is the most likely diagnosis?

A	Haemophilia A
B	Haemophilia B
C	Anti-phospholipid antibody syndrome
D	Von Willebrand's disease
E	Acquired haemophilia

21196

Question 32 of 139

A 64-year-old man presents with a first spontaneous haematoma in his right thigh. Past medical history of note includes rheumatoid arthritis, for which he takes sulphasalazine and low-dose prednisolone.

Investigations:

Hb	11.9 g/dl
WCC	6.1 × 10^9/l
PLT	201 × 10^9/l
Na^+	140 mmol/l
K^+	4.4 mmol/l
Creatinine	100 µmol/l
PT	15s (11.5-15.5)
APTT	41s (30-40)
Lupus anti-coagulant	-

Which of the following is the most likely diagnosis?

Your answer was correct

Question 32 of 139

E Acquired haemophilia

Acquired haemophilia is associated with anti-factor VIII IgG antibodies and is idiopathic in the majority of cases. In others there appears to be an association with other autoimmune diseases such as rheumatoid arthritis or inflammatory bowel disease, or with drugs such as phenytoin. Where there are low levels of the anti-factor VIII antibodies, factor VIII replacement may be all that is required. Where bleeding is a serious problem then immunosuppression with corticosteroids ± steroid-sparing agents such as ciclosporin may be required. Use of recombinant factor VII in patients with severe acquired haemophilia is a further potential option.

A Haemophilia A

APTT is prolonged in keeping with factor VIII deficiency, although haemophilia A would not present *de novo* at the age of 64.

B	Haemophilia B

Haemophilia B related to factor IX deficiency is associated with bleeding tendency, although like haemophilia A, it doesn't present for the first time at age 64.

C	Anti-phospholipid antibody syndrome

Anti-phospholipid antibody syndrome is associated with prolongation of the APTT, although it is associated with thrombosis rather than bleeding.

D	Von Willebrand's disease

In VWD the APTT is mildly prolonged in 50% of cases. Presentation at an earlier age than 64 would almost certainly be expected, however; hence the scenario here is much more consistent with acquired haemophilia.

21196

Question 1 of 107

An 18-year-old Caucasian with a 4-month history of non-specific chest pain is seen in your Outpatient Clinic. She had been having intermittent twinges that initially settled with mild analgesics, but they have become more frequent and painful of late. She is most aware of them just underneath her sternum and there is no radiation. Movement does not exacerbate the pain. However, the more severe pains make her feel dizzy and she has almost passed out on three occasions. There is no history of night sweats, weight loss or fever. She is not short of breath on exertion, but admits that recently she has been too tired to play sport. She does not smoke or take illicit drugs and has recently gone off alcohol. She had asthma as a child but rarely used her salbutamol inhaler. She is on the oral contraceptive pill and has a steady boyfriend.

On examination, she looks tired and slightly anxious. She is afebrile. Her pulse is 64 bpm and regular, BP 105/62 mmHg, respirations at rest 16 breaths/min and saturations 97% on

room air. She has a small lymph node in the left submandibular region. Heart sounds are normal, her chest is clear and her abdomen is soft with no enlarged organs. ECG shows sinus rhythm. Chest X-ray PA reveals an enlarged mediastinum, with clear lung fields; an anterior mediastinal mass can be seen on the lateral chest X-ray.

Investigations:

Hb	8.9 g/dl
WCC	6.4×10^9/l
PLT	165×10^9/l
Na^+	139 mmol/l
K^+	4.2 mmol/l
Creatinine	68 µmol/l
Urea	4.1 mmol/l
Glucose	4.9 mmol/l
LDH	1652 U/l
MCV	79.3 fl

Question 1 of 107

CT of the thorax, abdomen and pelvis reveals: a large anterior mediastinal mass with irregular borders, 10.1 cm × 9.3 cm × 5.6 cm, surrounding the left pulmonary artery and ligamentum arteriosum; no infiltration of surrounding tissues; a large group of lymph nodes in the left axilla; no abnormalities in the abdomen and pelvis.

Bone marrow biopsy shows non-specific fibrous tissue. What is the most likely diagnosis?

A Hodgkin's lymphoma

B Hairy cell leukaemia

C Malignant teratoma

D Thymoma

E Tuberculosis

2301

A Hodgkin's lymphoma

Hodgkin's lymphoma is a malignant proliferation of lymphocytes. Some 25% of patients have a constitutional upset (i.e. night sweats, weight loss, fever, pruritus and lethargy). Rarely, there may be alcohol-induced pain or features due to mass effects of the affected nodes. An isolated bone marrow biopsy may not yield any significant results as Hodgkin's disease can cause patchy bone marrow infiltration, Lymph node biopsies are often more useful. Reed–Sternberg cells are evident on microscopy. Treatment depends on classification and staging, but usually involves multiple chemotherapy agents. Prognosis is usually good.

B Hairy cell leukaemia

Patients with hairy cell leukaemia have infiltration of the bone marrow by malignant B lymphocytes (the 'hairy cells'). This leads to failure to produce

cells'). This leads to failure to produce red blood cells, white bloods cells and platelets. Leukaemic cells accumulate within the spleen, leading to massive splenomegaly. Fatigue is also a key sign. Not all patients with hairy cell leukaemia require treatment but, if they do, often single-agent treatment will suffice. This patient's presentation is not in keeping with a diagnosis of hairy cell leukaemia.

C Malignant teratoma

A differential for an anterior mediastinal mass includes teratoma. However, teratomas are extremely rare and are often associated with pelvic disease, which the patient in this case does not have. These are usually tumours that develop in utero but that are only picked up much later on in life. Diagnosis is usually via histology. Some teratomas contain yolk sac elements that secrete alpha-fetoprotein (AFP). However, AFP levels are more commonly used to monitor for disease recurrence after diagnosis rather than

teratomas contain yolk sac elements that secrete alpha-fetoprotein (AFP). However, AFP levels are more commonly used to monitor for disease recurrence after diagnosis rather than being diagnostic.

D	Thymoma

This patient has an anterior mediastinal mass which could be in keeping with a thymoma. However, the mass in this patient has irregular borders and usually with a thymoma you see a smooth, encapsulated tumour.

E	Tuberculosis

This patient has a clear lung fields on CT where you would normally expect to find lesions. The patient also is not suffering with temperatures, productive cough or haemoptysis, all of which make a diagnosis of TB less likely.

2301

Rate this question:

A 45-year-old man is referred from his general practitioner with an abnormal white cell count found on routine testing.

On examination, he has several 1–2 cm lymph nodes and 3 cm splenomegaly.

Investigations:

Hb	9.5g/dl
WCC	34.3 x 10^9/l
PLT	94 x 10^9/l
Lymphocytes	31 x 10^9/l

Immunophenotype was positive for B-cell markers (CD19 and CD20) with aberrant expression of the T-cell marker CD5.

What is the most likely diagnosis?

A	Acute myeloid leukaemia (AML)
B	Acute lymphoblastic leukaemia (ALL)

Question 2 of 107

Lymphocytes	31 x 10^9/l

Immunophenotype was positive for B-cell markers (CD19 and CD20) with aberrant expression of the T-cell marker CD5.

What is the most likely diagnosis?

A	Acute myeloid leukaemia (AML)
B	Acute lymphoblastic leukaemia (ALL)
C	Chronic lymphocytic leukaemia (CLL)
D	Chronic myeloid leukaemia (CML)
E	Non-Hodgkin's lymphoma (NHL)

6382

C Chronic lymphocytic leukaemia (CLL)

This man has an increase in mature lymphocytes in his peripheral blood. Immunophenotyping can be used to identify leucocytes by staining them with antibodies to the 'CD' (cluster differentiation) system, and is standard testing in unexplained lymphocytosis. Chronic lymphocytic leukaemia, a condition of B lymphocytes, paradoxically expresses CD5, a T-cell marker. Chronic lymphocytic leukaemia (CLL) can be staged according to two systems – Binet's and Rai's classifications – which use a combination of clinical features and number of cytopenia. Although Binet's stage A CLL (less than three sites of lymphadenopathy, normal platelets and haemoglobin) carries a normal life expectancy (and does not require treatment), this man has much more advanced disease with widespread lymphadenopathy and advanced marrow failure, and this is what drives the need to explain to him about

the need to explain to him about limited life expectancy. Recent advances have shown that positivity to ZAP (zeta-associated protein) 70 is associated with poorer prognosis disease.

B Acute lymphoblastic leukaemia (ALL)

ALL blood film examination reveals circulating blasts, and flow cytometry with cytogenetics can be used to differentiate ALL from AML. AML is usually associated with blasts that are positive for CD33, whereas ALL-associated cells are not.

A Acute myeloid leukaemia (AML)

Circulating blasts with markers on flow cytometry consistent with immature lymphocytes are found in the peripheral blood of patients with AML.

D Chronic myeloid leukaemia

Question 1 of 104

An 18-year-old woman presents with an episode of epistaxis, which settles with conservative management. Apparently she has had a recent flu-like illness.

On examination, she has a number of petechiae and some bruising where she has taken knocks or bangs to her legs. She is on no significant medication and has a clean past medical history. You understand that her aunt had a splenectomy as a young adult.

Investigations:

Hb	11.0 g/dl
WCC	5.0 x10^9/l
PLT	16.0 × 10^9/l
Na$^+$	139 mmol/l
K$^+$	4.0 mmol/l
Creatinine	105 µmol/l

Which of the following is the most appropriate treatment?

WCC	5.0 x10⁹/l
PLT	16.0 × 10⁹/l
Na^+	139 mmol/l
K^+	4.0 mmol/l
Creatinine	105 μmol/l

Which of the following is the most appropriate treatment?

A	Platelet transfusion
B	Prednisolone 20 mg daily
C	Prednisolone 60 mg daily
D	Splenectomy
E	Azathioprine 100 mg daily

20556

A 19-year-old woman presents with a 12 h history of sudden loss of power in the left arm. She is previously fit and well, smokes five cigarettes daily and is on the combined oral contraceptive pill. Her grandfather had a stroke in his eighties, and she has five siblings who are well.

Examination shows increased tone and brisk reflexes in the left arm. There is a 12 cm splenomegaly. Computed tomography of the head is normal.

Investigations:

Hb	12.3 g/dl
WCC	18.5 x 10^9/l
Platelets	1035 x 10^9/l

A blood film shows a left shift with markedly increased platelets, which vary significantly in size (anisothrombia). Bone marrow shows a translocation between chromosomes 9 and 22.

What is the most likely diagnosis?

Platelets	1035 x 10^9/l

A blood film shows a left shift with markedly increased platelets, which vary significantly in size (anisothrombia). Bone marrow shows a translocation between chromosomes 9 and 22.

What is the most likely diagnosis?

A	Essential thrombocythaemia with cerebrovascular accident
B	Antiphospholipid syndrome with reactive thrombocytosis
C	Cerebral lupus with reactive thrombocytosis
D	Chronic myelogenous leukaemia (CML)
E	Acute myeloid leukaemia

8255

D	Chronic myelogenous leukaemia (CML)

The history is compatible with a cerebrovascular accident, and the high platelet count is likely to be the cause. Chronic myelogenous leukaemia (a myeloproliferative disorder) usually manifests with thrombocytosis at presentation, usually with a raised white cell count that is grossly left-shifted (where promyelocytes, metamyelocytes and myelocytes are all visible on the peripheral blood). There is usually marked splenomegaly and the bone marrow is nearly always positive for the Philadelphia chromosome (the abnormally small chromosome 22 is the ‘Philadelphia’ chromosome). The basophil count is often increased in myeloproliferative disorders.

A	Essential thrombocythaemia with cerebrovascular accident

Essential thrombocythaemia can

A Essential thrombocythaemia with cerebrovascular accident

Essential thrombocythaemia can present with splenomegaly, but where the Philadelphia chromosome is found the disease is always classified as chronic myeloid leukaemia. There would not be a translocation of chromosomes 9 and 22 in essential thrombocythaemia.

B Antiphospholipid syndrome with reactive thrombocytosis

Platelet counts are characteristically low in anti-phospholipid syndrome, but are high in all the myeloproliferative disorders such as CML. Also, there would not be a translocation of chromosomes 9 and 22 in anti-phospholipid syndrome.

C Cerebral lupus with reactive thrombocytosis

Central lupus usually presents with low

Question 1 of 104

C	Cerebral lupus with reactive thrombocytosis

Central lupus usually presents with low platelets and pancytopenia. It can give rise to strokes, seizures or changes to the mental state. There would not be a translocation of chromosomes 9 and 22 in lupus.

E	Acute myeloid leukaemia

Acute myeloid leukaemia occurs when there is a maturational arrest in bone marrow cells early on in their development, leading to a variety of blood test results. These include thrombocytopenia, anaemia and low, high or normal white cell counts. Circulating blasts are seen on a blood film and there is no translocation of chromosomes with AML.

8255

Question 2 of 104

A 30-year-old man has been admitted for an elective knee arthroscopy. You are asked to review him prior to the operation. He has a past history of gallstones, and had jaundice as a child, but otherwise he is fit and well.

Examination reveals mild splenomegaly.

Investigations:

Hb	12.7 g/dl
WCC	8.2 × 10⁹/l
PLT	400 × 10⁹/l
MCV	78 fl
MCHC	43 g/dl (32-35 g/dl)
Reticulocytes	3.3% (0.5-2.4%)

What is the most likely diagnosis?

A	Sickle cell disease
B	Sideroblastic anaemia

Question 2 of 104

WCC	8.2 × 10^9/l
PLT	400 × 10^9/l
MCV	78 fl
MCHC	43 g/dl (32-35 g/dl)
Reticulocytes	3.3% (0.5-2.4%)

What is the most likely diagnosis?

A	Sickle cell disease
B	Sideroblastic anaemia
C	Iron deficiency anaemia
D	Thalassaemia trait
E	Hereditary spherocytosis

7074

E	Hereditary spherocytosis

Hereditary spherocytosis is inherited as an autosomal dominant condition and is one of the most common inherited haemolytic anaemias. The defect is in the membrane skeleton (usually the spectrin component), resulting in the appearance of spherocytes in the blood film. The spleen removes these spherocytes from the blood. Symptoms are variable in severity but include anaemia, jaundice and splenomegaly. With haemolysis, patients are at increased risk of pigment gallstones. The mean cell volume is usually low and the mean corpuscular haemoglobin concentration is usually high. The most sensitive test to confirm the diagnosis is the osmotic fragility test. Folic acid can be given to aid haemopoiesis, but occasionally splenectomy is required.

A	Sickle cell disease

Given that this patient is 30 years old,

Question 2 of 104

a history of sickle cell crisis would be expected in a patient with sickle cell disease.

B	Sideroblastic anaemia

Sideroblastic anaemia presents with more significant symptoms of anaemia than those reported here, and also leads to iron overload, which itself can present with cardiac failure and hepatic fibrosis/cirrhosis.

C	Iron deficiency anaemia

Iron deficiency anaemia is associated with microcytic anaemia. Although increased reticulocytes are associated with haemolytic anaemia, gallstones would not be expected.

D	Thalassaemia trait

Thalassaemia trait is generally associated with slightly lower MCV (in the 65–75 range) and is not associated with elevated reticulocytes.

Question 3 of 104

An 18-year-old man presents with sudden onset left-sided weakness of 24 h duration. He has sickle cell anaemia, and has required admissions in the past for management of chest crises. He is on ibuprofen for pain when necessary, penicillin V and folic acid. He smokes ten cigarettes daily and drinks 21 units of alcohol per week. His mother and father are both carriers for HbS, and he has no siblings or children.

On examination, he has dense, left-sided weakness, with brisk reflexes and up-going plantars on the left-hand side. Computed tomography (CT) of the brain confirms a right-sided hypodense lesion. His haemoglobin (Hb) is 110 g/l.

What is the most appropriate short-term intervention?

A Hydroxyurea

B 5′-Azacytidine

His mother and father are both carriers for HbS, and he has no siblings or children.

On examination, he has dense, left-sided weakness, with brisk reflexes and up-going plantars on the left-hand side. Computed tomography (CT) of the brain confirms a right-sided hypodense lesion. His haemoglobin (Hb) is 110 g/l.

What is the most appropriate short-term intervention?

A Hydroxyurea

B 5′-Azacytidine

C Bone marrow transplantation

D Thrombolytic therapy

E Exchange transfusion

6310

E Exchange transfusion

6–10% of sickle cell patients will suffer a stroke, usually during childhood. The risk can be predicted by transcranial Doppler measurement of the middle cerebral artery flow rate, and prompt institution of a prophylactic transfusion programme to reduce the HbS percentage can prevent future strokes. Silent infarcts can lead to reduced cognition and limited educational attainment. In this case, with symptoms of acute stroke, exchange transfusion is the most appropriate next step.

A Hydroxyurea

There is growing evidence that in addition to its effects on painful and chest crises, hydroxyurea may impact positively on the stroke rate in patients with sickle cell disease, although in the short term exchange transfusion is more effective.

Question 3 of 104

B	5′-Azacytidine

5′-Azacytidine is a DNA methylating agent that can improve HbF levels where hydroxyurea has failed, but it is cytotoxic and its use remains limited, particularly given the young age of this patient.

C	Bone marrow transplantation

Due to the high procedure-related mortality, transplant is usually only considered suitable for patients under 16 with a matched sibling donor; it is not considered superior to a transfusion therapy.

D	Thrombolytic therapy

24 h after symptoms began, this patient is outside the window for thrombolysis and this is therefore not an option.

6310

Rate this question: ☆☆☆☆☆

Question 4 of 104

A 70-year-old man presents with severe, unremitting epistaxis from both nostrils. The ENT registrar successfully packs the nose, but the patient complains of continuous post-nasal drip and has had several episodes of melaena. He has been suffering from prominent joint pains in the knees and hands for several months.

There is no previous medical history of note other than an uncomplicated hernia repair a year ago. Family history reveals nothing of significance. He is on no medication.

On examination, he has moderate synovitis of several proximal interphalangeal, metacarpo-phalangeal and large joints. Blood pressure is 90/60 mmHg, pulse 120 beats per minute (bpm), respiratory rate 25 breaths per minute. His skin is cool to the touch. He is covered in large bruises.

Investigations:

Hb	7.3 g/dl
WCC	4.3 × 10^9/l

bruises.

Investigations:

Hb	7.3 g/dl
WCC	4.3 × 10^9/l
PLT	556 × 10^9/l
ESR	74 mm/first hour
APTT (does not correct in mixing study)	75 s (30–40 s)
PT	12 s (11.5–15.5 s)
Factor VIII activity	Reduced

What is the most appropriate therapy for this man's bleeding?

A	Recombinant factor VIII
B	Recombinant factor IX

Question 4 of 104

ESR	mm/first hour
APTT (does not correct in mixing study)	75 s (30–40 s)
PT	12 s (11.5–15.5 s)
Factor VIII activity	Reduced

What is the most appropriate therapy for this man’s bleeding?

A	Recombinant factor VIII
B	Recombinant factor IX
C	Cryoprecipitate
D	FFP
E	Recombinant activated factor VII

6384

E Recombinant activated factor VII

Initially developed for use in patients with congential haemophilia with allo-antibody inhibitors, recombinant activated factor VII has been successfully used in patients with acquired haemophilia. It binds to the surface of activated platelets, where it supports thrombin generation and by-passes the need for FVIII.

A Recombinant factor VIII

This gentleman has an acquired factor VIII deficiency, probably associated with rheumatoid arthritis. Acquired haemophilia is more common in the elderly or during pregnancy, often in association with concurrent autoimmune disease or malignancy. It is due to an antibody to a coagulation factor, most commonly factor VIII, often referred to as an 'inhibitor'. Bleeding can be severe to the point that great care should be taken with

Bleeding can be severe to the point that great care should be taken with cannula insertion since compartment syndrome may ensue. Diagnosis is by performing mixing studies with patients and normal plasma: a simple factor deficiency will be corrected by mixing with normal plasma, but an acquired inhibitor will not correct with mixing. The inhibitor can then be measured by the Bethesda assay, which can be used to monitor response to treatment. Treatment with factor VIII is usually ineffective as the inhibitor has rapid activity.

B Recombinant factor IX

Recombinant factor IX is used in patients with inherited factor IX deficiency (haemophilia B). It isn't of significant utility in patients with acquired factor VIII deficiency.

C Cryoprecipitate

Cryoprecipitate, derived from FFP,

Recombinant factor IX is used in patients with inherited factor IX deficiency (haemophilia B). It isn't of significant utility in patients with acquired factor VIII deficiency.

C	Cryoprecipitate

Cryoprecipitate, derived from FFP, contains fibrinogen, von Willebrand factor, factor VIII, factor XIII and fibronectin, and is not likely to be effective here versus activated factor VII.

D	FFP

Given that FFP is a product derived from blood transfusion, it does contain factor VII, but recombinant activated factor VII is much preferred as it doesn't carry any risk of contamination.

6384

11:19

Question 5 of 104

A 71-year-old man with a long history of rheumatoid arthritis presents for review. He has recently complained of loss of weight and a number of episodes of dark urine, but normal stools. He admits to drinking 20 units of alcohol per week and has previously lived in the tropics, but has not travelled abroad recently.

On examination, he weighs 80 kg. There is a palpable spleen. His liver function tests were normal, apart from raised total bilirubin. Urine analysis showed urobilinogen, urosiderin, no bilirubin and no red blood cells. Haemoglobin was reduced at 10 g/dl, there was an increase in spherocytes, and both haptoglobins and platelets were reduced.

Which of the following is the next best investigation in this case?

A	Hepatic ultrasound scan
B	Endoscopic retrograde cholangiopancreatography

There is a palpable spleen. His liver function tests were normal, apart from raised total bilirubin. Urine analysis showed urobilinogen, urosiderin, no bilirubin and no red blood cells. Haemoglobin was reduced at 10 g/dl, there was an increase in spherocytes, and both haptoglobins and platelets were reduced.

Which of the following is the next best investigation in this case?

A	Hepatic ultrasound scan
B	Endoscopic retrograde cholangiopancreatography (ERCP)
C	Direct antiglobulin test
D	Bone marrow
E	Thick and thin film

33305

Question 5 of 104

stools. He admits to drinking 20 units of alcohol per week and has previously lived in the tropics, but has not travelled abroad recently.

On examination, he weighs 80 kg. There is a palpable spleen. His liver function tests were normal, apart from raised total bilirubin. Urine analysis showed urobilinogen, urosiderin, no bilirubin and no red blood cells. Haemoglobin was reduced at 10 g/dl, there was an increase in spherocytes, and both haptoglobins and platelets were reduced.

Which of the following is the next best investigation in this case?

Your answer was correct

A Hepatic ultrasound scan

B Endoscopic retrograde cholangiopancreatography (ERCP)

Question 5 of 104

C Direct antiglobulin test

This picture suggests the possibility of haemolytic anaemia. We are aware that he has a long history of rheumatoid arthritis, which is associated with increased haemolytic anaemia. Clinical pointers include spherocytosis as a result of red cell damage, positive direct antiglobulin test and the coexistence of autoimmune thrombocytopaenia. His weight loss is likely to be related to disease activity of his rheumatoid arthritis. Doses of prednisolone of 1 mg/kg are sufficient to induce remission in around 80% of cases. Other immunosuppressive drugs such as azathioprine and cyclophosphamide may be used in relapsed patients or in those who fail initial therapy. Splenectomy may be considered in patients with refractory disease.

A Hepatic ultrasound scan

The scenario points towards

A Hepatic ultrasound scan

The scenario points towards haemolysis. There are no signs/symptoms of liver disease. Patient reports dark urine with normal stool, thus excluding any relevance to hepatic pathology.

B Endoscopic retrograde cholangiopancreatography (ERCP)

There is no evidence of biliary system pathology. The raised bilirubin is secondary to haemolysis.

D Bone marrow

This investigation is invasive and will not aid the diagnosis, since all the tests needed to confirm haemolytic anaemia can be done on peripheral blood.

E Thick and thin film

hepatic pathology.

B	Endoscopic retrograde cholangiopancreatography (ERCP)

There is no evidence of biliary system pathology. The raised bilirubin is secondary to haemolysis.

D	Bone marrow

This investigation is invasive and will not aid the diagnosis, since all the tests needed to confirm haemolytic anaemia can be done on peripheral blood.

E	Thick and thin film

Malaria can be a cause for haemolysis, but there are no pointers in the clinical scenario towards that diagnosis.

33305

A 62-year-old man with chronic lymphatic lymphoma (CLL) presents to the GP complaining of increased shortness of breath and wheeze. He has a history of asthma for which he takes seretide, and he takes fludarabine for the CLL.

On examination, he is pyrexial 38.1 °C, and there is wheeze and coarse crackles on auscultation of the chest.

Investigation:

Hb	10.0 g/dl
WCC	17.9 × 10^9/l
PLT	92 × 10^9/l
Na^+	135 mmol/l
K^+	4.2 mmol/l
Creatinine	140 µmol/l
IgG	5.3 g/l (6.0-13.0)

Which of the following is the most appropriate prophylaxis against further pneumonia episodes?

Question 6 of 104

Na⁺	135 mmol/l
K⁺	4.2 mmol/l
Creatinine	140 µmol/l
IgG	5.3 g/l (6.0-13.0)

Which of the following is the most appropriate prophylaxis against further pneumonia episodes?

A	Immunoglobulin transfusion
B	Regular ciprofloxacin
C	Regular co-trimoxazole
D	Chlorambucil combination therapy
E	Alemtuzumab combination therapy

21527

C Regular co-trimoxazole

Patients who take fludarabine are at increased risk of infection with a range of pathogens including *Pneumocystis*, *Listeria*, *Neisseria* and *Legionella*. Both daily and thrice weekly regimens for dosing co-trimoxazole are effective.

A Immunoglobulin transfusion

Where IgG is markedly reduced, regular immunoglobulin transfusions may be required, although here IgG is only just below the lower limit of normal.

B Regular ciprofloxacin

Ciprofloxacin is a potentially useful prophylaxis against organisms such as *Listeria*, but it is not effective against *Pneumocystis*.

D Chlorambucil combination therapy

Ciprofloxacin is a potentially useful prophylaxis against organisms such as *Listeria*, but it is not effective against *Pneumocystis*.

D Chlorambucil combination therapy

Chlorambucil is likely to promote further immunosuppression when used in combination with fludarabine, and studies of the two combined showed no greater efficacy than fludarabine monotherapy in the treatment of CLL.

E Alemtuzumab combination therapy

Alemtuzumab targets lymphocytes bearing the CD52 cell surface protein. It is used as combination therapy for CLL, but it doesn’t reduce the risk of opportunistic infection.

Question 7 of 104

A 78-year-old man presents with sudden deterioration of vision in his left eye, with no eye pain. There are flame haemorrhages in one quadrant on retinal examination.

He has a history of hypertension and is awaiting investigations for anaemia; recent haemoglobin is 10.5 g/dl.

What diagnosis fits best with this clinical picture?

A	Branch retinal vein occlusion
B	Branch retinal artery occlusion
C	Central retinal vein occlusion
D	Central retinal artery occlusion
E	CMV retinitis

33308

Question 7 of 104

A	Branch retinal vein occlusion

Patients often complain of a sudden painless decrease of vision in the affected eye. Some patients may complain of a scotoma. Risk factors for retinal vein occlusion include systemic hypertension, hypertriglyceridaemia and hyperviscosity syndromes. Some inflammatory (e.g. sarcoidosis) and thrombophilic conditions (e.g. SLE) may also be involved. Management involves screening for risk factors and anticoagulation. Further management depends on which underlying condition has been identified.

B	Branch retinal artery occlusion

This is usually embolic in aetiology. Patients with branch retinal artery occlusion typically present with acute, unilateral, painless, partial visual loss. Visual field defects may be central or sectoral. Patients may also be asymptomatic. Risk factors include

sectoral. Patients may also be asymptomatic. Risk factors include smoking, hypertension, hypercholesterolaemia, diabetes, coronary artery disease and history of stroke or transient ischemic attack.

C Central retinal vein occlusion

Patients can be either asymptomatic or present with decreased vision, photophobia and painful or red eyes. Fundoscopy shows tortuosity and dilatation of all branches of the central retinal vein, dot/blot and flame-shaped hemorrhages, throughout all four quadrants and most numerous in the periphery, and optic disc and macular oedema. This tends to be more severe in ischaemic CRVO than non-ischaemic CRVO.

D Central retinal artery occlusion

This is embolic in aetiology. The most common presenting complaint is an acute, persistent, painless loss of vision

appear normal. The classic findings of retinal whitening and a cherry red spot are due to opacification of the nerve fibre layer as it becomes oedematous from ischeamia. The fovea is cherry red because it has no overlying nerve fibre layer. This finding may take hours to develop, and the oedema is associated with a worse visual prognosis. Over the course of about a month, the inner retina becomes atrophic as the swelling resolves

E	CMV retinitis

Presenting symptoms vary depending on the location of retinal involvement. Posterior lesions present with diminished visual acuity. More peripheral lesions initially can be asymptomatic. Floaters often are noted if significant vitreitis is present. The eye usually is white and quiet. In immunocompromised individuals, CMV most commonly presents as a viral necrotising retinitis with a characteristic ophthalmoscopic appearance.

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A 49-year-old woman presents with fatigue. She has chronic kidney diease (CKD) secondary to systemic lupus erythematosus, requiring dialysis for the last three years. She is on prednisolone 20 mg daily and erythropoietin alpha 3500 units three times weekly.

Examination is unremarkable other than noticeable pallor.

Investigations:

Hb	4.9 g/dl
WCC	3.5 × 10^9/l
PLT	455 × 10^9/l
Neutrophils	3.0 × 10^9/l
MCV	83 fl (80–96)
Reticulocytes	13 × 10^9/l (25–85)
Serum B_{12}	163 ng/l (160–760)
Serum folate	5 µg/l (2.0–11.0)
	Plentiful megakaryocytes,

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Serum folate	5 µg/l (2.0–11.0)
Bone marrow	Plentiful megakaryocytes, normal myeloid maturation, absent erythropoiesis and no infiltrates

What is the most likely diagnosis?

A	Diamond Blackfan anaemia
B	Anaemia of chronic disease
C	Lupus-associated myelofibrosis
D	Paroxysmal nocturnal haemoglobinuria
E	Pure red cell aplasia

6298

Question 8 of 104

(CKD) secondary to systemic lupus erythematosus, requiring dialysis for the last three years. She is on prednisolone 20 mg daily and erythropoietin alpha 3500 units three times weekly.

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Serum folate	5 µg/l (2.0–11.0)
Bone marrow	Plentiful megakaryocytes, normal myeloid maturation, absent erythropoiesis and no

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E	Pure red cell aplasia

Pure red cell aplasia is diagnosed when there is unexplained anaemia and reticulocytopenia, with a complete absence of red cell precursors in the bone marrow but with preservation of other cell lines. It can occur spontaneously, or in association with autoimmune diseases, lymphoproliferative disorders or viral illnesses such as HIV, hepatitis and herpes. Treatment is supportive, with immunosuppression. Rarely, the condition can occur where recombinant erythropoietin is administered and patients respond to withdrawal of erythropoietin.

A	Diamond Blackfan anaemia

Diamond Blackfan anaemia is an inherited pure red cell aplasia which would present in infancy rather than in the fifth decade. Diagnosis is made via a full blood count and bone marrow biopsy. Treatment is with

biopsy. Treatment is with corticosteroids and transfusions as required. Bone marrow transplantation can also be considered. This diagnosis is unlikely due to the patient presenting in their 40s.

B	Anaemia of chronic disease

Anaemia of chronic disease is a possibility in a patient with SLE who is requiring dialysis. To be able to diagnose an anaemia of chronic disease, we would need to have carried out transferrin saturations (high) and ferritin levels (normal/high). Also it is usual for a patient on dialysis to have regular bloods, in which case the ongoing anaemia would have been picked up earlier.

C	Lupus-associated myelofibrosis

Myelofibrosis can be seen in lupus, but the bone marrow is characteristically a dry tap and marked fibrosis is seen on

12:18

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Myelofibrosis can be seen in lupus, but the bone marrow is characteristically a dry tap and marked fibrosis is seen on the bone marrow trephine.

D Paroxysmal nocturnal haemoglobinuria

Classically presents with red discoloration of urine. However, a patient on dialysis may not produce any urine. Other symptoms include anaemia, abdominal pain, difficulty in swallowing and thrombosis. Diagnosis is usually by bloods in keeping with an intravascular haemolytic anaemia (raised bilirubin and LDH and low Hb and haptoglobin) and a positive Ham test (with increased RBC fragility indicating PNH). Treatment is usually with steroids and transfusions, as required.

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Rate this question: ⊖ ☆☆☆☆☆

Next Question

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A 63-year-old man is admitted to Accident and Emergency with a 5-day history of vomiting, diarrhoea and bloody stools. The diarrhoea and vomiting stopped 2 days ago, but he noticed his abdomen was distended and had constant colicky pain. He also complains of dyspnoea on minimal exertion and increasing urinary frequency, with small volumes of urine. Apart from attending a wedding reception a week ago, he has only eaten home-made food. He has hypertension and gout and takes an ACE inhibitor, calcium-channel blocker, allopurinol and a statin. He is a non-smoker but enjoys a bottle of red wine at weekends.

On examination, he is pale and slightly agitated. His temperature is 37.1 °C, pulse 96 regular, BP 142/92 mmHg. His respirations are 24 breaths/min at rest and his saturations are 96% on room air. His heart sounds are normal but basal crackles can be heard on chest examination. His abdomen is distended and tympanic, mildly tender and bowel sounds are reduced. Rectal

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sounds are reduced. Rectal examination reveals a brown stool.

Investigations:

Hb	9.8 g/dl
WCC	28.7 × 10^9/l
PLT	65 × 10^9/l
Na^+	130 mmol/l
K^+	4.7 mmol/l
Creatinine	8462 µmol/l
Urea	40.8 mmol/l
Albumin	12 g/l
Bilirubin	100 µmol/l
ALT	60 U/l
ALP	61 U/l
MCV	91 fl
LDH	1240 U/l
CRP	354 mg/l

CRP	354 mg/l

The blood film shows schistocytes and burr cells.

Chest X-ray reveals alveolar shadowing at both bases, with small bilateral pleural effusions.

What is the diagnosis?

A	Crohn’s colitis
B	Gastroenteritis
C	Haemolytic–uraemic syndrome
D	Polyarteritis nodosa
E	*Legionella* pneumonia

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C Haemolytic–uraemic syndrome

HUS is characterised by the triad of micro-angiopathic haemolytic anaemia, thrombocytopenia and acute kidney disease. Typically, HUS occurs after a prodrome of diarrhoea. In adults, HUS is usually caused by the enterohaemorrhagic serotypes of *Escherichia coli,* especially *E. coli* O157:H7. The source of the infection is usually contaminated beef, poultry or cider, although faecal-to-hand transmission can occur. HUS is associated with: malignant hypertension; infection (e.g. *E. coli, Shigella* spp, HIV); vasculitis; radiation nephritis; collagen vascular diseases (e.g. scleroderma); cryoglobulinaemia; malignancy, mainly adenocarcinoma; drugs (e.g. oral contraceptive therapy, chemotherapy, ciclosporin); bone marrow transplantation; eclampsia; and postpartum acute kidney disease.

Uraemia cannot explain all the haematological findings in this case, particularly the presence of schistocytes and burr cells on the blood film. These indications of micro-angiopathic anaemia suggest red cell trauma due to fibrin deposition in the microvasculature. When thrombotic micro-angiopathy involves the kidneys, thrombosis of glomerular capillaries and renal arterioles can lead to kidney disease. In the severe form of the disease, bilateral cortical necrosis and irreversible kidney disease may occur. Plasmapheresis with fresh-frozen plasma as the replacement fluid is the current treatment of choice. Renal replacement therapy might also be required.

Some patients can have atypical HUS. This is an extremely rare, progressive and potentially life-threatening condition seen in both children and adults and which often (70%) has a genetic component. It can also be referred to as diarrhoea-negative HUS. It is commonly caused by mutations in the complement regulatory proteins

the complement regulatory proteins causing a chronic, uncontrolled activation of the complement system leading to systemic thrombotic micro-angiopathy which ultimately causes sudden or progressive damage to vital organs. Historically, approximately 40% of patients died or developed chronic kidney disease following their first episode of atypical HUS. Subsequent episodes led to 65% of patients dying, requiring dialysis or suffering long-term renal damage in spite of plasma exchange.

More recently, eculizumab has been used in patients with atypical HUS. Eculizumab is a human monoclonal antibody, produced from murine myeloma cells, that binds to complement C5 and blocks pro-thrombotic and pro-inflammatory processes. It has been found to improve renal function, reduce thrombotic micro-angiopathic activity and improve patient quality of life, although there is a lack of randomised controlled trials.

Crohn’s usually presents in 15–25-year-olds, although there is a second peak at around 55–70 years. As in this patient’s case, the presentation is one of severe diarrhoea and abdominal tenderness with distension. Patients often also suffer with perianal fistulae and mouth ulcers. This patient is unlikely to have Crohn’s disease as the diarrhoea lasted only 48 h and also, after this point, the patient noted increased urinary frequency. If the patient had Crohn’s colitis, you would expect ongoing diarrhoea (possibly bloods) with acute kidney disease as a result of fluid depletion secondary to diarrhoea.

B Gastroenteritis

You may have considered gastroenteritis as a possible diagnosis given the history of a recent meal out with subsequent diarrhoea lasting 24–48 h. However, gastroenteritis would not explain the subsequent increase in urinary frequency.

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D Polyarteritis nodosa

PAN is a necrotising arteritis of small and/or medium vessels without glomerulonephritis. Patients often present with skin lesions, mononeuritis multiplex and involvement of the GI tract, heart, central nervous system and kidneys, as well as myalgia. Bloods show a hypergammaglobulinaemia, leucocytosis and raised neutrophil count. The mainstay of treatment is with corticosteroids. This patient is unlikely to have PAN as you would expect a raised protein level, and although GI and renal symptoms can be present, these are less common compared to the incidence in other diseases.

E *Legionella* pneumonia

If the patient had a *Legionella* pneumonia you would expect them to have a cough and fevers in addition to the hyponatraemia, auscultation findings and dyspnoea. This also doesn't fully explain his abdominal

count. The mainstay of treatment is with corticosteroids. This patient is unlikely to have PAN as you would expect a raised protein level, and although GI and renal symptoms can be present, these are less common compared to the incidence in other diseases.

E	*Legionella* pneumonia

If the patient had a *Legionella* pneumonia you would expect them to have a cough and fevers in addition to the hyponatraemia, auscultation findings and dyspnoea. This also doesn't fully explain his abdominal findings or bloody diarrhoea. *Legionella* pneumonia could be on your differentials but is not a unifying diagnosis for this patient's findings.

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A 52-year-old woman is bought to her GP by her carer who has become concerned after noticing that the patient's gums have progressively become more prominent over the last few months. She tried to take the patient to the dentist but no NHS dental appointments were available. The patient lives in a home since she has learning difficulties.

Her past medical history is unremarkable except for three infections in the last 6 weeks. The carer has also noticed that recently the patient has become increasingly fatigued by even the lightest of activities and is commonly short of breath on exertion. She is not currently on any medications but has taken various courses of antibiotics recently.

On examination, she is noted to be anaemic and has multiple bruises over her body. She has hypertrophic bleeding gums and, on auscultation of the heart, she is found to have a flow murmur. She has mild splenomegaly on palpation of her abdomen. Routine blood tests were requested and

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palpation of her abdomen. Routine blood tests were requested and confirmed the presence of anaemia, a raised white cell count, low neutrophil count and thrombocytopenia. A blood film shows increased numbers of blast cells and the presence of Auer rods.

Given these findings, what is the most likely diagnosis?

A Acute myeloid leukaemia (AML)

B Acute lymphoblastic leukaemia (ALL)

C Chronic myeloid leukaemia (CML)

D Chronic lymphoid leukaemia (CLL)

E Chronic myelomonocytic leukaemia (CMML)

Question 10 of 104

On examination, she is noted to be anaemic and has multiple bruises over her body. She has hypertrophic bleeding gums and, on auscultation of the heart, she is found to have a flow murmur. She has mild splenomegaly on palpation of her abdomen. Routine blood tests were requested and confirmed the presence of anaemia, a raised white cell count, low neutrophil count and thrombocytopenia. A blood film shows increased numbers of blast cells and the presence of Auer rods.

Given these findings, what is the most likely diagnosis?

Your answer was correct

A Acute myeloid leukaemia (AML)

B Acute lymphoblastic leukaemia (ALL)

C Chronic myeloid leukaemia (CML)

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A	Acute myeloid leukaemia (AML)

Acute myeloid leukaemia (AML) is a malignant disease of the bone marrow in which the blast cells derived from the myeloid marrow elements undergo a neoplastic proliferation. AML is distinguished by the presence of >20% blasts in the blood and/or bone marrow. It is more common in men and the prevalence increases with age, but it can affect all age groups. It is, however, becoming more common as a long-term complication of chemotherapy. Symptoms are usually related to marrow failure (anaemia, infections, bleeding) and/or organ infiltration with leukaemic cells (bone pain, hepatosplenomegaly, gum hypertrophy, proptosis), but patients can also have constitutional symptoms (weakness, fever, lethargy).

B	Acute lymphoblastic leukaemia (ALL)

AML is differentiated from ALL by the

AML is differentiated from ALL by the presence of Auer rods, which are eosinophilic needle-like cytoplasmic inclusions found in blast cells and that are pathognomonic of AML.

C Chronic myeloid leukaemia (CML)

CML is a myeloproliferative disorder characterised by the proliferation of the precursors for white blood cells, but these precursors retain the ability to differentiate. Symptoms tend to be chronic and the blood profile shows an increased (++) white cell count, with a low or normal haemoglobin and a variable platelet count.

D Chronic lymphoid leukaemia (CLL)

The most noteworthy laboratory abnormality found in CLL is lymphocytosis in the peripheral blood and bone marrow. Although the absolute blood lymphocyte threshold

absolute blood lymphocyte threshold for diagnosing CLL has been placed at >5000/microl (5 × 10^9/l) B lymphocytes, a significant proportion of patients presents with counts as high as 100,000/microl (100 × 10^9/l). The peripheral blood smear of patients with CLL demonstrates a lymphocytosis. The leukemic cells are typically small, mature-appearing lymphocytes with a dense nucleus, partially aggregated (clumped) chromatin and lacking discernible nucleoli. There is a narrow border of clear to slightly basophilic cytoplasm. The blood film in this scenario is not that of CLL.

E	Chronic myelomonocytic leukaemia (CMML)

CMML is characterised by a progressive cytopenia in the presence of a hypercellular bone marrow and usually involves all three cell lines (myeloid/monocyte, erythroid, megakaryocyte).

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A 30-year-old woman with known sickle cell disease (SC phenotype) presents with severe abdominal pain. She has had multiple admissions in the past for abdominal pain, requiring large doses of parenteral opiates. She has not had any chest crises or strokes in the past.

She is on folic acid 5 mg daily, penicillin V 250 mg twice daily, morphine sulphate slow-release 200 mg twice daily with 80 mg morphine sulphate for breakthrough pains. She works as a nurse in intensive care and has two children aged 8 and 10, who are both well. Her brother died from sickle cell disease 1 year ago.

On examination, her blood pressure is 132/82, pulse is 88 and regular. Her temperature is 38.4 °C. She is in extreme pain, particularly in the upper region of her abdomen.

Investigations:

Hb	6.4 g/dl
WCC	$13.3 \times 10^9/l$

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Hb	6.4 g/dl
WCC	13.3 × 10⁹/l
PLT	403 x 10⁹/l
Bilirubin	135 µmol/l (1–22)
ALP	235 U/l

What do you think is the most likely cause of this patient's abdominal pain?

A	Opiate-seeking behaviour
B	Splenic sequestration crisis
C	Vaso-occlusive sickle-cell crisis
D	Cholecystitis
E	Transfusion-associated hepatitis

Question 11 of 104

She is on folic acid 5 mg daily, penicillin V 250 mg twice daily, morphine sulphate slow-release 200 mg twice daily with 80 mg morphine sulphate for breakthrough pains. She works as a nurse in intensive care and has two children aged 8 and 10, who are both well. Her brother died from sickle cell disease 1 year ago.

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What do you think is the most likely cause of this patient’s abdominal pain?

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D Cholecystitis

The patient has severe abdominal pain with obstructive jaundice. The bilirubin is too high to be due to chronic haemolysis, and the raised alkaline phosphatase fits better with hepatic obstruction rather than a vaso-occlusive crisis. The raised white count and pyrexia further support cholecystitis as the underlying diagnosis. Cholecystitis is more common in patients with sickle cell disease due to chronic haemolysis.

C Vaso-occlusive sickle-cell crisis

Vaso-occlusive sickle cell crisis may present with chest or abdominal pain, but the obstructive picture on LFTs and pyrexia don't fit with a diagnosis of vaso-occlusive crisis.

A Opiate-seeking behaviour

Great care should be taken before

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Great care should be taken before deciding that a patient is truly addicted to opioids. Addiction has a variety of definitions, but usually implies abnormal behaviour to gain access to a drug, either with craving or compulsive use or use despite harmful effects of a drug. Sickle cell patients are often tolerant to opioids – requiring large doses to obtain a therapeutic effect and occasionally dependent – developing withdrawal effects if opioids are stopped suddenly.

B	Splenic sequestration crisis

Splenic infarction is progressive in patients with sickle cell disease, meaning that splenic sequestration crisis becomes rarer as age increases.

E	Transfusion-associated hepatitis

Transfusion-associated hepatitis isn't associated with an acute presentation with acute abdominal pain, but with features of chronic liver disease

A 50-year-old woman undergoes routine cholecystectomy. Her preoperative full blood count was normal and her operative progress was unremarkable other than a small postoperative bleed that settled with simple pressure to the wound. You are asked to see her, as she has become confused. She has no previous medical history of note and works as a computer programmer.

On examination, she is disorientated in time and place. Temperature 37.9 °C, pulse 110 beats per minute (bpm), blood pressure 110/70 mmHg, respiratory rate 24 breaths per minute. Heart sounds are normal and jugular venous pressure is not raised. Chest reveals some bronchial breathing on the right lower and middle zones. Her O_2 saturation is 91% on air. Abdominal examination reveals mild tenderness around the operative scar but is otherwise normal.

Investigations:

Hb	9.5 g/dl

Investigations:

Hb	9.5 g/dl
WCC	12.3 × 10⁹/l
PLT	790 × 10⁹/l
Na⁺	139 mmol/l
K⁺	4.5 mmol/l
Creatinine	197 µmol/l
CRP	272

A blood film shows a dramatic increase in platelets with many enlarged forms. There is an increase in left-shifted granulocytes including metamyelocytes, myelocytes and promyelocytes.

In addition to basic resuscitation, what action would you take?

A	Aspirin 300 mg with ceftazidime 1 g twice daily intravenously

increase in platelets with many enlarged forms. There is an increase in left-shifted granulocytes including metamyelocytes, myelocytes and promyelocytes.

In addition to basic resuscitation, what action would you take?

A	Aspirin 300 mg with ceftazidime 1 g twice daily intravenously
B	Aspirin 75 mg plus hydroxyurea 1 g twice daily
C	Apheresis to reduce the platelet count urgently
D	Anticoagulation with heparin to therapeutic levels
E	Levofloxacin intravenously

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Na^+	139 mmol/l
K^+	4.5 mmol/l
Creatinine	197 µmol/l
CRP	272

E Levofloxacin intravenously

This patient has developed postoperative pneumonia, which is making her confused secondary to hypoxia. The platelet count is raised secondary to infection – the normal preoperative count makes a primary haematological diagnosis unlikely in the extreme; the left shift is also secondary to infection. First-line therapy in this situation is usually a quinolone, accompanied by metronidazole if there is evidence of aspiration.

B Aspirin 75 mg plus hydroxyurea 1 g twice daily

Hydroxyurea with aspirin is standard treatment for essential thrombocytosis, a clonal stem cell disorder associated with increased risk of thrombosis and haemorrhage.

A Aspirin 300 mg with

	ceftazidime 1 g twice daily intravenously

Aspirin is not required in this situation given that the increased platelet count is reactive; ceftazidime is an appropriate antibiotic choice where *Pseudomonas* is suspected.

C	Apheresis to reduce the platelet count urgently

Given that the platelet count increase is reactive as a result of ongoing infection, there is no indication for apheresis to take place.

D	Anticoagulation with heparin to therapeutic levels

Anticoagulation with heparin to therapeutic levels isn't indicated, and may in the postoperative period increase the risk of haemorrhage. Prophylactic dosing with low-molecular weight heparin may, however, be used here.

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A 74-year-old patient presents to the GP with headache, dizziness, vertigo, vague abdominal pain and general lethargy. He has previously been fit and well, with mild hypertension as his only significant past medical history. On examination his BP is 155/95 mmHg and he has a ruddy complexion.

Investigations:

Hb	17.9 g/dl
WCC	19.5 x10^9/l
PLT	450 x10^9/l
Na^+	141 mmol/l
K^+	4.9 mmol/l
Creatinine	145 µmol/l
Haematocrit	0.56

You suspect primary polycythaemia. Which of the following investigations is most likely to provide a diagnosis?

A LDH levels

Question 13 of 104

PLT	450 x10^9/l
Na$^+$	141 mmol/l
K$^+$	4.9 mmol/l
Creatinine	145 µmol/l
Haematocrit	0.56

You suspect primary polycythaemia. Which of the following investigations is most likely to provide a diagnosis?

A	LDH levels
B	JAK-2 mutation testing
C	Arterial blood gas estimation
D	Uric acid levels
E	C282Y mutation testing

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B	JAK-2 mutation testing

JAK-2 mutation testing is widely available, with the V617F mutation being found in approximately 96% of patients with primary polycythaemia. The protein is a signalling protein within the JAK-STAT pathway, which drives production of red blood cells.

A	LDH levels

Although LDH levels are elevated in the presence of haematological malignancy, they are non-specific so could not be used to confirm a diagnosis of primary polycythaemia here.

C	Arterial blood gas estimation

Absence of hypoxia makes secondary polycythaemia less likely, although in conditions such as obesity hypoventilation syndrome, where hypoxia is more marked at night, hypoxia may be missed in the clinic.

A 37-year-old nurse presents to the ENT Department with a flu-like illness. She gives a 10-year history of tendency to have a blocked, stuffy nose and frequent recurrent coughs and colds.

The Occupational Health team has also noticed that she failed to show a response to hepatitis B and tetanus vaccinations.

In which immunoglobulin is she likely to be deficient?

A	IgA
B	IgE
C	IgD
D	IgM
E	IgG

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Question 14 of 104

A 37-year-old nurse presents to the ENT Department with a flu-like illness. She gives a 10-year history of tendency to have a blocked, stuffy nose and frequent recurrent coughs and colds.

The Occupational Health team has also noticed that she failed to show a response to hepatitis B and tetanus vaccinations.

In which immunoglobulin is she likely to be deficient?

Your answer was correct

A IgA

B IgE

C IgD

D IgM

E IgG

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A	IgA

This patient is most likely to have IgA deficiency, which is particularly associated with recurrent sinus infections due to encapsulated bacteria such as *Haemophilus influenzae*. Selective IgA deficiency is probably the most common of the primary immunodeficiency disorders, but it may also be asymptomatic. In Caucasians, IgA deficiency is said to occur in 1 in 600–700 individuals. There is often a deficient response to polysaccharide-based vaccinations. In patients with IgA deficiency, 10–44% of patients may have anti-IgA antibodies; this risks a severe reaction to IgA-containing products such as blood, plasma or immunoglobulin.

B	IgE

There are few case reports in the literature regarding IgE deficiency.

C	IgD

IgD immunodeficiency is quite rare, and individuals with this condition do not seem to be predisposed to infections.

D	IgM

Sometimes, in cases of IgA deficiency, compensatory IgM increase may occur.

E	IgG

IgG immunodeficiency is also common. IgG-subclass deficiency and its importance have been characterised. Antibodies against pneumococcal polysaccharide antigens are predominantly IgG2 and, to a lesser degree, IgG4. Antibodies against protein antigens, such as tetanus, are predominantly IgG1 and, to a lesser degree, IgG3. Finally, antibodies against large extracellular parasites, such as *Schistosoma* and *Filaria* organisms, exclusively belong to the

infections.

D IgM

Sometimes, in cases of IgA deficiency, compensatory IgM increase may occur.

E IgG

IgG immunodeficiency is also common. IgG-subclass deficiency and its importance have been characterised. Antibodies against pneumococcal polysaccharide antigens are predominantly IgG2 and, to a lesser degree, IgG4. Antibodies against protein antigens, such as tetanus, are predominantly IgG1 and, to a lesser degree, IgG3. Finally, antibodies against large extracellular parasites, such as *Schistosoma* and *Filaria* organisms, exclusively belong to the IgG4 subclass. The history of sinus infections in the present scenario points towards IgA immunodeficiency.

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A 62-year-old woman presents to her GP complaining of lethargy. Past history includes hypertension, for which she takes amlodipine and bendroflumethiazide, osteoarthritis for which she takes paracetamol, recurrent urinary tract infections for which she is currently taking a 6-week course of cephalexin, and epilepsy for which she takes sodium valproate.

On examination, she looks pale and her skin is yellow-tinged. Her pulse is 100 bpm and regular, and her BP is 110/70 mmHg. Direct Coomb's test is positive; serum haptoglobins are low; reticulocyte count is elevated. Urine dipstick is positive for blood. You suspect haemolysis.

Which of the following agents is most likely to be responsible?

A Paracetamol

B Sodium valproate

C Cephalexin

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Which of the following agents is most likely to be responsible?

A Paracetamol

B Sodium valproate

C Cephalexin

D Amlodipine

E Bendroflumethiazide

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Which of the following agents is most likely to be responsible?

Your answer was correct

A Paracetamol

B Sodium valproate

C Cephalexin

C Cephalexin

The more common causes of drug-induced haemolytic anaemia include penicillin and penicillin derivatives, cephalosporins, levodopa, methyldopa, quinidine and some non-steroidal anti-inflammatory agents. Discontinuing the causative agent usually leads to a rapid improvement in the condition, and a short course of oral prednisolone may accelerate recovery. The underlying condition most frequently associated with drug-induced haemolytic anaemia is G6PD deficiency, an X-linked condition which occurs most frequently in men of black, Asian or Mediterranean origin.

A Paracetamol

The main concern with respect to use of paracetamol is hepatic failure rather than haemolytic anaemia. Given that this is a widely used over-the-counter medication, it has an excellent safety profile.

B	Sodium valproate

Sodium valproate can cause anaemia, but this is related to bone marrow abnormalities rather than to haemolytic anaemia. These bone marrow abnormalities resolve on discontinuation of the medication.

D	Amlodipine

Amlodipine in rare cases is associated with reductions in the white blood cell count and/or low platelets.

E	Bendroflumethiazide

Blood dyscrasias are rarely reported in patients treated with thiazides, although these are not related to haemolytic anaemia.

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A 73-year-old man attends the clinic complaining of headaches and dizziness. He also complains of generalised lethargy and sweating, predominantly at night.

On examination, he has a plethoric ruddy complexion, bruising and there is splenomegaly on abdominal examination. His blood pressure is elevated at 155/90 mmHg.

Investigations:

Hb	18.5 g/dl
WCC	10.2 x 10^9/l
PLT	456 x 10^9/l
Na$^+$	140 mmol/l
K$^+$	4.9 mmol/l
Creatinine	150 µmol/l

You wonder about a possible diagnosis of primary polycythaemia.

Which of the following is the most specific test to confirm a diagnosis of

Na⁺	140 mmol/l
K⁺	4.9 mmol/l
Creatinine	150 µmol/l

You wonder about a possible diagnosis of primary polycythaemia.

Which of the following is the most specific test to confirm a diagnosis of primary polycythaemia?

A	Ferritin levels
B	JAK2 screening
C	Erythropoeitin levels
D	JNK2 screening
E	Arterial blood gasses

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B JAK2 screening

JAK2 mutation screening is most specific for the diagnosis of primary polycythaemia. JAK2 is a crucial tyrosine kinase which transmits the EPO signal to increase red cell production. The majority of PCV is caused by a mutation in the gene coding for JAK2, which leads to red cell production independent of EPO levels. A small number of other mutations leading to PCV have also now been identified.

A Ferritin levels

Ferritin levels are usually low in primary polycythaemia, although a normal ferritin wouldn't necessarily rule out the diagnosis.

C Erythropoeitin levels

These are generally suppressed in primary polycythaemia, although where there is co-existent hypoxia they

normal ferritin wouldn't necessarily rule out the diagnosis.

C	Erythropoeitin levels

These are generally suppressed in primary polycythaemia, although where there is co-existent hypoxia they may be in the normal range.

D	JNK2 screening

JNK2 is a protein kinase activated by a variety of environmental stressors including UV radiation.

E	Arterial blood gasses

Arterial blood gases are useful when secondary polycythaemia is suspected because of the existence of hypoxia.

21031

Question 17 of 104

An 89-year-old woman is an inpatient recovering from community-acquired pneumonia. She is on warfarin for atrial fibrillation, and has been put on intravenous ampicillin since admission 48 hours ago.

You are contacted for advice regarding management of her high international normalised ratio (INR). She is currently well, with no symptoms or signs of bleeding. INR > 10 (target 2.5).

What is the most appropriate management?

A Observation alone

B 5 mg of oral vitamin K or 0.5–1 mg of IV vitamin K

C 15 ml/kg of fresh frozen plasma

D 10 units of cryoprecipitate

E Prothrombin complex

Question 17 of 104

You are contacted for advice regarding management of her high international normalised ratio (INR). She is currently well, with no symptoms or signs of bleeding. INR > 10 (target 2.5).

What is the most appropriate management?

Your answer was correct

A Observation alone

B 5 mg of oral vitamin K or 0.5–1 mg of IV vitamin K

C 15 ml/kg of fresh frozen plasma

D 10 units of cryoprecipitate

E Prothrombin complex concentrate containing

B 5 mg of oral vitamin K or 0.5–1 mg of IV vitamin K

It will take several days for the INR to fall to a safe level, and patients over 70 years of age are at increased risk of haemorrhagic complications. Also at risk of haemorrhage are patients who already have minor bleeding. e.g. gum bleeding or epistaxis, or those who have bled in the past on warfarin. Both oral and IV vitamin K are potential options with an INR >8, without active bleeding at the doses described above (5 mg oral, or 0.5–1 mg IV).

A Observation alone

At an INR >10, spontaneous and potentially significant bleeding can be seen at any time. As such, intervention with vitamin K is required.

C 15 ml/kg of fresh frozen plasma

C	15 ml/kg of fresh frozen plasma

A level of 15 ml/kg of fresh frozen plasma is unlikely to raise coagulation factors above 20%: higher doses, while more likely to correct adequately, can cause fluid overload. Fresh frozen plasma is not virally inactivated and can cause transfusion complications such as transfusion-related acute lung injury. As such other options for acute correction of INR related to warfarin excess are preferred.

D	10 units of cryoprecipitate

Cryoprecipitate contains higher levels of factor VIII and fibrinogen: its use is therefore limited mainly to the treatment of dysfibrinogenaemia or hypofibrinogenaemia.

E	Prothrombin complex concentrate containing factors II, VII, IX and X

injury. As such other options for acute correction of INR related to warfarin excess are preferred.

D	10 units of cryoprecipitate

Cryoprecipitate contains higher levels of factor VIII and fibrinogen: its use is therefore limited mainly to the treatment of dysfibrinogenaemia or hypofibrinogenaemia.

E	Prothrombin complex concentrate containing factors II, VII, IX and X

Prothrombin complex concentrate is extremely useful for rapidly reversing over-anticoagulation with warfarin, but it is a pooled plasma product and can cause disseminated intravascular coagulation: its use is therefore in life-threatening bleeding associated with over-anticoagulation.

6304

A 33-year-old woman is admitted to hospital with a 1-week history of dark urine and severe fatigue. On further questioning she admits to increasing tiredness over a matter of weeks.

One day before admission, she developed severe abdominal pain and abdominal distension. On examination, she has pallor, jaundice, an enlarged tender liver and ascites.

Investigations:

Hb	7.9 g/dl
WCC	3.2 x 10^9/l
Platelets	89 x 10^9/l
MCV	101 fl
Peripheral smear	Mild polychromasia
AST	144 U/l
ALT	130 U/l
Bilirubin	54 µmol/l
Urine	++

Bilirubin	54 µmol/l
Urine Haemosiderin	++
Urobilinogen	+

Abdominal ultrasound reveals an enlarged liver, ascites and absent flow in the hepatic veins.

What single test would you request to confirm the underlying diagnosis?

A	Viral hepatitis serology
B	Liver biopsy
C	Inherited thrombophilia screen
D	Flow cytometry for CD55 and CD59 expression
E	Glucose-6-phosphate dehydrogenase (G6PD) assay

D Flow cytometry for CD55 and CD59 expression

This patient has paroxysmal nocturnal haemoglobinuria (PNH) complicated by acute hepatic vein thrombosis (Budd–Chiari syndrome). PNH is an acquired clonal disorder of haematopoietic stem cells, characterised by a variable combination of intravascular haemolysis, thrombosis and bone marrow failure. A somatic mutation in the phosphatidylinositol glycan-A (PIG-A) gene on the X chromosome leads to deficiency of several glycosyl-phosphatidylinositol (GPI)-linked molecules. Deficiency of decay accelerating factor (DAF, CD55) and the membrane inhibitor of reactive lysis (MIRL, CD59) increases susceptibility to complement-mediated lysis of blood cells. Currently, diagnosis is made by flow cytometric evaluation of blood, which confirms the CD55 and CD59 deficiencies and deficiency of expression of other GPI-linked proteins. This test is replacing older,

proteins. This test is replacing older, complement-based assays (such as Ham's test and the sucrose lysis test) because it is less affected by blood transfusion, is more sensitive and specific and it measures the size of the PNH clone, which is useful for follow-up.

A Viral hepatitis serology

This patient does not have viral hepatitis. Although with similar presentation symptoms of fatigue, dark urine, abdominal pain and jaundice, there would not be a disturbance of flow across the hepatic veins or evidence of haemolysis or anaemia.

B Liver biopsy

A liver biopsy would not be diagnostic for PNH. It may show evidence of scarring or fibrosis. There is a high risk of bleeding with liver biopsies and, with low platelets and altered liver

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C	Inherited thrombophilia screen

PNH is an acquired condition. It is not inherited and so would not give a diagnosis of PNH on testing for inherited thrombophilias. It is likely that a thrombophilia screen would be largely negative. One study has shown an increase in anti-phospholipid antibody in some patients with PNH, although it is unsure how this affects the patient.

E	Glucose-6-phosphate dehydrogenase (G6PD) assay

Looking for G6PD deficiency is not appropriate in this instance. G6PD deficiency does produce haemolysis and jaundice but it is an X-linked inherited condition unlike PNH, which is acquired and doesn't affect males and females differently.

8590

Rate this question: ☆☆☆☆☆

A 34-year-old woman attends the Anticoagulant Clinic as she is on warfarin for recurrent emboli. Her first pulmonary embolus arose after hospitalisation for fixation of a fractured tibia four years previously. She has had at least three further episodes since then. She has not yet had children but wishes to conceive and is concerned about the effects of warfarin.

What is the most appropriate advice for her regarding the possibility of conception and pregnancy?

A	Continue warfarin but change to low-molecular weight heparin within six weeks of conception
B	Replace warfarin with low-dose aspirin and use additional low-molecular weight heparin during the first trimester and the postpartum period

heparin within six weeks of conception

B Replace warfarin with low-dose aspirin and use additional low-molecular weight heparin during the first trimester and the postpartum period

C Switch to aspirin until the birth of the child then revert to warfarin

D Stop warfarin immediately and replace with low-molecular weight heparin

E Stop warfarin and consider low-molecular weight heparin if she has a further thromboembolic event

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D	Stop warfarin immediately and replace with low-molecular weight heparin

Warfarin is teratogenic and should be avoided in the first trimester of pregnancy. Warfarin not be used before the sixth week of pregnancy to minimise the risk of fetal abnormalities. In an ideal situation stopping warfarin prior to conception could be preferable, but in reality may elevate the risk of thrombotic events (even if heparin was substituted) during an undefined, and possibly long, period while this patient waited to become pregnant because of less good compliance with injectable therapy. As this woman is high risk for further pulmonary emboli, she should be converted to low-molecular weight heparin for the duration of her pregnancy. However, it should be noted that in this difficult clinical situation, for which inadequate evidence is available on which to base clinical decision making, the risk–benefit ratio must be judged on an

benefit ratio must be judged on an individual case basis to some extent.

A	Continue warfarin but change to low-molecular weight heparin within six weeks of conception

Warfarin is teratogenic and should be avoided in the first trimester of pregnancy. Warfarin should be stopped before the sixth week of pregnancy to minimise the risk of fetal abnormalities.

B	Replace warfarin with low-dose aspirin and use additional low-molecular weight heparin during the first trimester and the postpartum period

As this woman is high risk for further pulmonary emboli, she should be converted to low-molecular weight heparin for the duration of her pregnancy, rather than just during first trimester and postpartum only.

pregnancy, rather than just during first trimester and postpartum only.

C Switch to aspirin until the birth of the child then revert to warfarin

As this woman is high risk for further pulmonary emboli, she should be converted to low-molecular weight heparin for the duration of her pregnancy.

E Stop warfarin and consider low-molecular weight heparin if she has a further thromboembolic event

As this woman is high risk for further pulmonary emboli, she should be converted to low-molecular weight heparin for the duration of her pregnancy. It would be prudent to prevent a thromboembolic event rather than to treat it when it occurs, as we already know she is high risk.

71094

Question 20 of 104

A 65-year-old man is admitted to hospital with confusion. His wife says he has been complaining of abdominal pain and, in his confused state, suffered a head injury. He has a background of angina.

Examination is difficult, but unremarkable.

Observations:

Blood pressure	110/60 mmHg
Heart rate	120 bpm, regular

Investigations:

Haemoglobin (Hb)	9.6 g/dl
White blood cells (WBC)	4.9 × 10^9/l
Platelets (PLT)	360 × 10^9/l
Sodium (Na^+)	135 mmol/l
Potassium (K^+)	4.6 mmol/l
Urea	12.2 mmol/l
Creatinine (Cr)	132 µmol/l

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Urea	12.2 mmol/l
Creatinine (Cr)	132 µmol/l
Calcium	3.6 mmol/l
Electrocardiogram (ECG)	Reduced QT interval

A skull X-ray done in Accident and Emergency shows multiple lytic lesions.

What is the most important initial step?

A	Bendroflumethiazide
B	Furosemide
C	Prednisolone
D	Intravenous (IV) fluids
E	IV bisphosphonate

D	Intravenous (IV) fluids

This patient has hypercalcaemia, most likely due to metastatic cancer or multiple myeloma. Patients are described as presenting with bone pain, renal stones, confusion and abdominal pain (bones, stones, psychic moans and abdominal groans). IV fluids can lead to a modest, but relatively rapid, fall in serum calcium, so this would be the first option here.

A	Bendroflumethiazide

Thiazide diuretics reduce calcium excretion and are therefore likely to further increase calcium levels in this situation.

B	Furosemide

Loop diuretics do reduce serum calcium, but in the presence of dehydration, their use is not advised, and IV fluids are the preferred initial intervention

Loop diuretics do reduce serum calcium, but in the presence of dehydration, their use is not advised, and IV fluids are the preferred initial intervention.

C	Prednisolone

Steroids do lower serum calcium, more modestly where there is an underlying solid neoplasm versus a haematological malignancy, but they take a number of hours to do this.

E	IV bisphosphonate

IV bisphosphonates are appropriate but take 1–2 days before their use is associated with a significant fall in serum calcium.

33296

A 40-year-old man presented to his GP with fatigue.

Investigations:

Hb	11.2 g/dl
WBC	5.6 x 10^9/l
PLT	360 x 10^9/l
Serum Ferritin	12 μg/l (15-300)

He was commenced on iron sulphate tablets for presumed iron deficiency anaemia. The GP has referred him to the Outpatient Clinic. The patient still feels fatigued, but also complains of numbness and tingling in the lower limbs. He recalls having an operation on his abdomen a few years ago while abroad for severe abdominal pain and upper GI haemorrhage, but cannot recall the specifics of the surgery. Otherwise, he has been fit and well.

Examination reveals pale conjunctivae and a lemon-yellow tinge to his skin. He has slight distal lower limb sensory loss and absence of ankle jerks with

loss and absence of ankle jerks with exaggerated knee reflexes. Abdominal examination shows a longitudinal median scar, but no organomegaly.

Repeat investigations:

Hb	10.4 g/dl
WBC	4.5×10^9/l
PLT	250×10^9/l
MCV	112 fl

Which operation is he most likely to have had?

A	Hemicolectomy
B	Terminal ileal resection
C	Pancreaticoduodenectomy
D	Splenectomy
E	Partial gastrectomy

E Partial gastrectomy

The patient has combined iron deficiency and B_{12} deficiency. A gastrectomy can cause this scenario. Gastric acid helps iron in the ferric form to be absorbed by enhancing solubility; without it, iron absorption is therefore reduced. Vitamin B_{12} is best absorbed in the terminal ileum when combined with intrinsic factor, which is produced by gastric parietal cells. Partial gastrectomy is likely to have driven a significant reduction in intrinsic factor production.

A Hemicolectomy

Hemicolectomy should not significantly impact on either B_{12} or ferritin absorption.

B Terminal ileal resection

Although terminal ileal resection does result in B_{12} deficiency and bile salt malabsorption, it should not lead to

Although terminal ileal resection does result in B_{12} deficiency and bile salt malabsorption, it should not lead to significant iron deficiency.

C	Pancreaticoduodenectomy

Pancreaticoduodenectomy isn’t performed for severe upper GI haemorrhage, but is performed for resectable pancreatic or ampulla of Vater carcinomas.

D	Splenectomy

Emergency splenectomy is performed for trauma, not for acute upper GI haemorrhage. It is also not associated with B_{12} or iron deficiency.

7075

Question 22 of 104

A 50-year-old man is referred to clinic by his general practitioner (GP). He recently suffered a fracture of his right humerus, with minimal trauma.

He has been complaining of increasing tiredness over the past few weeks and months and has been unable to continue his job working in a builder’s merchants.

Bloods taken at the GP practice prompted his referral:

Haemoglobin (Hb)	8.9 g/dl
White blood cells (WBC)	9.5 × 10^9/l
Platelets (PLT)	140 × 10^9/l
Mean corpuscular volume (MCV)	86 fl
Erythrocyte sedimentation rate (ESR)	60 mm/first hour
Sodium (Na^+)	149 mmol/l
Potassium (K^+)	3.6 mmol/l

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Urea	15 mmol/l
Creatinine (Cr)	160 µmol/l
Calcium (corrected)	2.89 mmol/l
Albumin	28 g/l
Total protein	89 g/l

An X-ray of the right humerus reported as a possible pathological fracture.

What next investigation would best help to confirm the diagnosis?

A	Chest X-ray
B	Radioisotope bone scan
C	Immunoglobulin electrophoresis
D	Prostate-specific antigen
E	Serum alkaline phosphatase

C Immunoglobulin electrophoresis

The most likely diagnosis with anaemia, raised ESR, hypercalcaemia, renal impairment and raised total protein with low albumin is multiple myeloma. This is a B-cell malignancy, resulting in paraproteinaemia. The diagnosis is confirmed by showing the presence of paraproteins, > 10% of plasma cells in the bone marrow and lytic bone lesions.

A Chest X-ray

The significant elevation in total protein and hypercalcaemia fit much better with multiple myeloma vs an underlying chest malignancy.

B Radioisotope bone scan

Radioisotope bone scans are insensitive, with respect to identifying lytic lesions in myeloma.

Radioisotope bone scans are insensitive, with respect to identifying lytic lesions in myeloma.

D Prostate-specific antigen

Although a polyclonal increase in immunoglobulins may be seen in patients with prostatic malignancy, the magnitude of increase seen here is much more consistent with a diagnosis of multiple myeloma.

E Serum alkaline phosphatase

Alkaline phosphatase levels are significantly lower in patients with multiple myeloma vs patients with solid tumour bony metastases.

33298

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An 18-year-old Cypriot tourist is admitted to A&E with severe abdominal pain. Over the last few days he had been coughing up green sputum and had pleuritic chest pain. He was given ciprofloxacin for presumed infection. This morning he awoke with sharp, very painful abdominal pain, worst in the epigastric area. No other symptoms. He drinks socially and doesn’t smoke.

On examination, he is jaundiced and in pain. His temperature is 39.5 °C, pulse 120 bpm, BP 102/48 mmHg and his respirations are 20 breaths/min. His saturations on room air are 95%. Some crackles and bronchial breathing at the right base can be heard. His abdomen is generally tender on palpation but with no guarding. Chest X-ray shows shadowing at the right lung base; ECG shows sinus tachycardia.

Investigations:

Hb	6.2 g/dl
WCC	17.3×10^{9}/l
PLT	465×10^{9}/l

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PLT	465 × 10^9/l
Na^+	136 mmol/l
K^+	4.5 mmol/l
Creatinine	84 µmol/l
Urea	4.5 mmol/l
Glucose	5.7 mmol/l
Albumin	38 g/l
Bilirubin	71 µmol/l
ALT	62 U/l
ALP	124 U/l
Amylase	45 U/l
MCV	97 fl
LDH	1256 U/l
Urine	Urobilinogen+
Blood film	Heinz bodies and bite cells noted

What is the diagnosis?

ALP	124 U/l
Amylase	45 U/l
MCV	97 fl
LDH	1256 U/l
Urine	Urobilinogen+
Blood film	Heinz bodies and bite cells noted

What is the diagnosis?

A G6PD deficiency

B Familial Mediterranean fever

C Atypical pneumonia

D Acute intermittent porphyria

E Acute pancreatitis

2298

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A G6PD deficiency

G6PD deficiency is the commonest red blood cell enzyme defect. It is a condition that is X-linked recessive in inheritance and is commonly found in Mediterranean and African populations. It is often triggered by infections, certain drugs (including ciprofloxacin), certain foods (including broad beans) and, at times, there can be no identifiable trigger. When exposed to an oxidative crisis there is typically a rapid. Patients are often noted as having anaemia, Heinz bodies on blood film (due to haemolysis), an elevated LDH and reduced haptoglobin levels. The mainstay of treatment is supportive measures. In chronic disease, it may be appropriate to consider a splenectomy.

B Familial Mediterranean fever

Familial Mediterranean fever (FMF) is an autosomal recessive disease that is more commonly found in

Question 24 of 104

A 25-year-old man presented with a 2-month history of drenching night sweats and weight loss of 6 kg. During history taking, he denied any foreign travel, diarrhoea or cough.

Clinical examination revealed a 2 cm lymph node in the right supraclavicular fossa. There was no hepatosplenomegaly.

Investigations:

Hb	11.2 g/l
WCC	5.3 × 109/l (85% neutrophils, 8% eosinophils)
PLT	160 × 10^9/l
CXR	Mediastinal mass (5 cm)
Abdominal ultrasound	Normal

What is the most likely diagnosis?

A Non-Hodgkin’s lymphoma

Question 24 of 104

WCC	5.3 × 109/l (85% neutrophils, 8% eosinophils)
PLT	160 × 10^9/l
CXR	Mediastinal mass (5 cm)
Abdominal ultrasound	Normal

What is the most likely diagnosis?

A	Non-Hodgkin’s lymphoma
B	Hodgkin’s lymphoma
C	Seminoma
D	Thymoma
E	Aspergilloma

33315

B	Hodgkin's lymphoma

The incidence of Hodgkin's lymphoma peaks in the age grouos 15–34 and >50 years, whereas non-Hodgkin's lymphoma is much commoner in older patients. For this reason, the clinical picture fits much more closely with Hodgkin's lymphoma. Hodgkin's disease is a neoplasm of lymphoid tissue that is defined histopathologically by the presence of malignant Reed–Sternberg cells with an appropriate cellular background. For an adequate sample of tissue, a formal biopsy is needed, and in this case the most accessible tissue would be from the supraclavicular fossa node. Constitutional symptoms may accompany the diagnosis of Hodgkin's disease. Patients with fever in excess of 38°C, drenching night sweats and weight loss exceeding 10% of baseline body weight during the 6 months preceding diagnosis are designated as having 'B' symptoms.

A typical presentation is the observation, usually by the patient, of

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observation, usually by the patient, of a painless, enlarging mass, most often in the neck, but occasionally in the axilla or inguinal-femoral region. In other patients, a chest X-ray demonstrates a moderate or even massive mediastinal enlargement with associated lower cervical lymphadenopathy.

A Non-Hodgkin’s lymphoma

About 85% of all malignant lymphomas are NHLs. The median age at diagnosis is the sixth decade of life, although Burkitt lymphoma and lymphoblastic lymphoma occur in younger patients. Low-grade lymphomas do not usually present with beta symptoms, as opposed to intermediate- and high-grade lymphomas.

C Seminoma

Seminomas account for one third of testicular germ cell tumours (GCTs), which are the most common

testicular germ cell tumours (GCTs), which are the most common malignancy in men aged 15–35 years. The most common sign at presentation is a painless testicular mass.

D Thymoma

Of patients with a thymoma, one third to one half are asymptomatic and one third present with local symptoms related to tumour encroachment on surrounding structures. These patients may present with cough, chest pain, superior vena cava syndrome, dysphagia and hoarseness if the recurrent laryngeal nerve is involved. One third of cases are found incidentally on radiographic examinations during a work-up for myasthenia gravis.

E Aspergilloma

Aspergilloma may manifest as an asymptomatic radiographic abnormality in a patient with pre-

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dysphagia and hoarseness if the recurrent laryngeal nerve is involved. One third of cases are found incidentally on radiographic examinations during a work-up for myasthenia gravis.

E	Aspergilloma

Aspergilloma may manifest as an asymptomatic radiographic abnormality in a patient with pre-existing cavitating lung disease due to sarcoidosis, tuberculosis or other necrotising pulmonary processes. It may also occur in cystic areas resulting from prior *Pneumocystis jirovecii* pneumonia in patients with HIV infection. The clinical presentation includes haemoptysis, which may be massive and life-threatening, in 40–60% of patients and, less commonly, cough and fever.

33315

A 62-year-old man has been referred by his GP for investigation of weight loss and night sweats. He has a history of treated hypertension and angina.

Examination reveals painless enlarged bilateral axillary lymph nodes. The other lymph node regions are normal. He also has splenomegaly.

Investigations:

Hb	12.0 g/dl
WBC	4.4 x 10^9/l
PLT	320 x 10^9/l
MCV	82 fl
Lymph node biopsy	Reed Sternberg cells with a nodules divided by collagen bands
Staging computed tomography (CT) scan	Axillary lymph nodes and splenomegaly

What is the stage of this disease with

Lymph node biopsy	Reed Sternberg cells with a nodules divided by collagen bands
Staging computed tomography (CT) scan	Axillary lymph nodes and splenomegaly

What is the stage of this disease with regards to the Ann Arbor classification?

A	II A
B	II B
C	III A
D	III B
E	IV

7069

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D III B

This patient is classified as having stage III B Hodgkin’s lymphoma because of the presence of axillary lymph nodes, splenomegaly and ‘B’ symptoms – in this case, significant weight loss coupled with night sweats. Pel–Ebstein fever has been described, where patients have a swinging pyrexia in 1–2-weekly cycles. Characteristically the Reed–Sternberg cell is found on biopsy and there are four subtypes on histology (nodular-sclerosing, mixed cellularity, lymphocyte-depleted, lymphocyte-rich).

E IV

Extra-nodal involvement, such as involvement of the liver and bone marrow, is required to fulfil the criteria for stage IV disease.

A II A

The fact there is splenic enlargement

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A	II A

The fact there is splenic enlargement moves the staging from II to III here, because there is disease on both sides of the diaphragm.

B	II B

Although there are B symptoms reported here, the presence of disease above and below the diaphragm means this is stage III rather than stage II disease.

C	III A

The presence of significant night sweats and weight loss precipitating presentation to the doctor, means this patient has ‘B’ disease.

7069

Question 26 of 104

You are asked to review the case of a 68-year-old woman who has had a lengthy dental procedure earlier in the day. She has a background of angina.

Current medications are isosorbide mononitrate and co-trimoxazole for a resistant urinary tract infection. She is complaining of a headache and breathlessness.

Examination shows her to be cyanosed.

Arterial blood gas on a 15 l non-rebreathe O_2 mask:

pH	7.42
P_aO_2	39.2 kPa
P_aCO_2	4.1 kPa
O_2 sats	70%
Portable chest X-ray	Normal appearance

What is the most likely diagnosis?

P_aCO_2	4.1 kPa
O_2 sats	70%
Portable chest X-ray	Normal appearance

What is the most likely diagnosis?

A	Aspiration
B	Carbon monoxide poisoning
C	Methaemoglobinaemia
D	Pulmonary embolism
E	Glucose-6-phosphate dehydrogenase (G6PD) deficiency

7071

C Methaemoglobinaemia

Haemoglobin carries iron in its ferrous form (Fe^{2+}). When it is converted to the ferric form (Fe^{3+}) methaemoglobin is created. This reduces the red cells' ability to carry oxygen. The body has a normal reparative mechanism involving reduced nicotinamide adenine dinucleotide phosphatase (NADPH), which reduces Fe^{3+} to Fe^{2+}. This mechanism is not fully operational in infants, making them susceptible to methaemoglobinaemia.

Drugs that provide oxidative stress, such as local anaesthetics (especially on mucosae), sulphonamides and nitrates can induce methaemoglobinaemia. Symptoms include headache, confusion, breathlessness and chest pain. Patients are cyanosed with no obvious cardiorespiratory cause, and despite increased oxygen delivery the oxygen saturations remain low. The blood is described as chocolate brown in colour and can be tested for

described as chocolate brown in colour and can be tested for methaemoglobin levels. Treatment is with methylene blue. If unsuccessful, exchange transfusion can be employed.

A	Aspiration

Given that the P_aO_2 is reported as 39.2 kPa on 15 l/min, aspiration is very unlikely. There is also no report of any vomiting or possible mechanism for aspiration during the procedure.

B	Carbon monoxide poisoning

Carbon monoxide poisoning is not associated with cyanosis, but rather with a cherry red skin coloration.

D	Pulmonary embolism

There is no history of chest pain to suggest pulmonary embolism, and it would be extremely unusual to have

B Carbon monoxide poisoning

Carbon monoxide poisoning is not associated with cyanosis, but rather with a cherry red skin coloration.

D Pulmonary embolism

There is no history of chest pain to suggest pulmonary embolism, and it would be extremely unusual to have onset of a PE in such a short period after immobility in the dentist's chair.

E Glucose-6-phosphate dehydrogenase (G6PD) deficiency

We are told this patient has a history of angina and is taking a nitrate. Nitrates may precipitate haemolysis in G6PD deficiency, and theiruse in this patient therefore counts against G6PD and acute haemolysis as a potential cause of her symptoms.

7071

You are asked to see a 30-year-old man who is undergoing inpatient treatment for acute myeloid leukaemia. He completed combination chemotherapy 6 days ago and was well until this morning when he noticed increasing breathlessness.

On examination, he is pale and clammy, with a high respiratory rate. Pulse is 130 bpm, blood pressure 110/70 mmHg, and his skin is cool to touch. He is slightly drowsy and disorientated. Temperature is 35.6 °C, and he has several crops of black lesions over his arms and legs. A chest X-ray is unremarkable.

Blood tests are shown below:

		Normal values
Haemoglobin (Hb)	73 g/l	
White cell count (WCC)	0.2 × 10^9/l	
Platelets (PLT)	13 × 10^9/l	

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Neutrophils	0 × 10^9/l	
Urea	10.3 mmol/l	2.5–7.5

A platelet transfusion is arranged.

Which other measure would you instigate?

A Biopsy the skin lesions

B Commence voriconazole

C Take blood and urine cultures and start antibiotics when results are available

D Commence broad-spectrum antibiotics with antipseudomonal cover

E Transfuse packed red cells to maintain Hb level above 100 g/l

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D | Commence broad-spectrum antibiotics with antipseudomonal cover

This patient is developing septic shock. The black lesions on the skin are ecthyma gangrenosum, a cutaneous manifestation of *Pseudomonas aeruginosa* infection. Given a WCC of 0.2 and neutrophil count of 0, commencement of broad-spectrum antibiotics with antipseudomonal cover, according to local guidelines, is the intervention of choice.

A | Biopsy the skin lesions

Invasive procedures, including skin biopsy, should be avoided in patients with neutropenia; in this case, a clinical diagnosis can be made.

B | Commence voriconazole

In this situation, antibacterials are usually commenced first, with antifungal cover added in patients who

D Commence voriconazole

In this situation, antibacterials are usually commenced first, with antifungal cover added in patients who fail to respond after 48 h.

C Take blood and urine cultures and start antibiotics when results are available

This risks a significant delay in treating any associated bacterial sepsis and a significantly increased risk of mortality.

E Transfuse packed red cells to maintain Hb level above 100 g/l

Surviving sepsis guidelines suggest a target of 70 g/l for Hb is adequate.

33295

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Ecthyma gangrenosum: Presentation in a normal neonate

Figure 1, Figure 2

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Multiple ecthyma gangrenosum lesions associated with Pseudomonas septicemia.

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A 34-year-old man with a history of minimal change glomerulonephritis presents to the Emergency Department with a swollen right lower leg.

Medication includes ramipril 10 mg daily and furosemide. He has recently spent a few hours on a flight home from Italy.

On examination, he has an obvious right DVT and his BP is 145/82 mmHg.

Investigations:

Hb	13.1 g/dl
WCC	8.2 x 10^9/l
PLT	231 x 10^9/l
Na^+	141 mmol/l
K^+	4.8 mmol/l
Urea	12.1 mmol/l
Creatinine	170 µmol/l
Albumin	23 g/l

Which of the following is the most

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K^+	4.8 mmol/l
Urea	12.1 mmol/l
Creatinine	170 µmol/l
Albumin	23 g/l

Which of the following is the most likely cause of his thrombosis?

A	Factor V Leiden mutation
B	Antithrombin III deficiency
C	Protein C deficiency
D	Hyperviscosity due to volume depletion
E	Anti-phospholipid antibody syndrome

21452

B Antithrombin III deficiency

This patient has significant protein loss and is taking furosemide in an attempt to control the resultant peripheral oedema. Whilst volume depletion increases the risk of peripheral thrombosis, the more likely cause is loss of antithrombin III into his urine because of nephrotic range proteinuria. Management in this case would involve anti-coagulation with warfarin therapy.

A Factor V Leiden mutation

Factor V Leiden is a variant of factor V, which cannot be easily degraded by activated protein C. This leads to hypercoagulability and increased risk of venous thromboembolism.

C Protein C deficiency

No significant reduction in protein C is seen in nephrotic syndrome. Protein C deficiency is genetic, and it is inherited

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C Protein C deficiency

No significant reduction in protein C is seen in nephrotic syndrome. Protein C deficiency is genetic, and it is inherited in autosomal dominant fashion.

D Hyperviscosity due to volume depletion

Although hyperviscosity due to volume depletion does impact on risk of DVT in patients with nephrotic syndrome, antithrombin III deficiency is likely to have the greater impact here.

E Anti-phospholipid antibody syndrome

Although co-existent anti-phospholipid antibody syndrome is theoretically possible, it is more likely to be associated with systemic lupus erythematosus.

21452

Rate this question:

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A 52-year-old woman presents with lethargy and easy bruising. She has also noticed breathlessness on exertion and has lost 4 kg in weight over the past couple of months. She was treated with curative intent for early-stage breast cancer 5 years ago and has been well since. She is on no medication. There is no other significant previous medical history.

Examination shows a thin woman with bruises on all extremities and pale conjunctiva but is otherwise normal.

Investigations:

Hb	9.9 g/dl
WCC	3.5 × 10^9/l
PLT	113 × 10^9/l
Neutrophils	1.0 × 10^9/l
Reticulocytes	13 × 10^9/l (25–85 × 10^9/l)
PT	12 s (11.5–15.5s)
aPTT	35 s (30–40)

aPTT	35 s (30–40)
Blood film	Band forms, myelocytes and occasional promyelocytes as well as nucleated red blood cells

What diagnosis would best fit this picture?

A	Acute promyelocytic leukaemia
B	Invasion of bone marrow by breast cancer
C	Myelofibrosis
D	Thrombotic thrombocytopaenic purpura
E	Aplastic anaemia

B	Invasion of bone marrow by breast cancer

The patient's blood tests show a leucoerythroblastic anaemia (left-shifted granulocytic series and nucleated red blood cells) with pancytopaenia. This can be seen with high bone marrow turnover, e.g. in severe haemolytic anaemia (in which case the reticulocyte count would be high), myelofibrosis and chronic myeloid leukaemia or bone marrow invasion. Often in bone marrow invasion the invading malignancy will already have been diagnosed previously, i.e. breast cancer in this case. The diagnosis requires a bone marrow trephine, which will usually show replacement of haematopoietic tissue with malignant cells.

A	Acute promyelocytic leukaemia

In APML, which is a subtype of acute myeloid leukaemia, the blood film would show myeloblasts with Auer

There would usually be a raised platelet count and either leukopaenia or leucocytosis with myelofibrosis. A blood film would show a leuco-erythroblastic picture but be associated with teardrop poikilocytes. Splenomegaly is often present on examination.

D	Thrombotic thrombocytopaenic purpura

TTP presents with neurological and psychological disturbances, thrombocytopenia, reduced renal function and haemolytic anaemia. Schistocytes or helmet cells are seen on a blood film.

E	Aplastic anaemia

Aplastic anaemia does cause pancytopenia but does not show a leuco-erythroblastic blood film. It is a result of haemopoietic stem cell failure in the bone marrow.

7600

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A 70-year-old man presents with a 200 ml fresh haematemesis. He is managed with long-term warfarin therapy for chronic atrial fibrillation and is usually on a stable dose of 4 mg per day.

Most recently, he has been prescribed a course of ciprofloxacin for a dental abscess.

On admission, his BP is 100/65 mmHg, with a pulse of 110/min.

Investigations:

Hb	10.0 g/dl
WCC	4.9 x 10^9/l
PLT	120 x 10^9/l
Na^+	139 mmol/l
K^+	5.9 mmol/l
Creatinine	185 μmol/l
INR	8.7 (<1.4)

Which of the following is most appropriate to reverse his

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Na^+	139 mmol/l
K^+	5.9 mmol/l
Creatinine	185 µmol/l
INR	8.7 (<1.4)

Which of the following is most appropriate to reverse his coagulopathy?

A Recombinant factor VIIa

B FFP

C Prothrombin complex concentrate (PCC)

D IV vitamin K

E Protamine sulphate

20633

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C Prothrombin complex concentrate (PCC)

This patient is in significant danger of massive haemorrhage and circulatory collapse. Intervention with PCC, targeted at rapidly reversing warfarin specifically, is therefore the intervention of choice.

A Recombinant factor VIIa

Recombinant factor VIIa has a role in partial reversal of factor Xa anticoagulants rather than warfarin. It may also have a role in treatment of patients with acquired haemophilia.

B FFP

FFP is less effective in reversing anticoagulation than PCC; it is therefore the default choice only when PCC is not available.

D IV vitamin K

patients with acquired haemophilia.

B	FFP

FFP is less effective in reversing anticoagulation than PCC; it is therefore the default choice only when PCC is not available.

D	IV vitamin K

IV vitamin K does reverse warfarin-related coagulopathy, although its onset of action is much slower versus PCC.

E	Protamine sulphate

Protamine sulphate is given as the antidote for excess heparinisation.

20633

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A 72-year-old man attends clinic for investigation of anaemia. He has noticed occasional episodes of dark urine, especially in the morning. He reports that he recently was admitted and treated for a portal vein thrombosis, and he now takes regular dalteparin. Other than that, he takes gliclizide for diabetes.

Examination reveals pale conjunctivae; his blood pressure is 132/89 mmHg, with pulse 75 and regular. Heart sounds are normal, the abdomen is soft and non-tender, and he has soft calves bilaterally.

Investigations:

Hb	11.2 g/dl (135–180)
WBC	3.9 × 10^9/l (4.0–11.0)
PLT	150 × 10^9/l (150–450)
Plasma haptoglobin	0.09 g/l (0.3–2.0)
PT	12s (11–14)
APTR	35 s (24–37)

calves bilaterally.

Investigations:

Hb	11.2 g/dl (135–180)
WBC	3.9 × 10^9/l (4.0–11.0)
PLT	150 × 10^9/l (150–450)
Plasma haptoglobin	0.09 g/l (0.3–2.0)
PT	12s (11–14)
APTR	35 s (24–37)
INR	1.0 (0.7–1.3)
Bilirubin	45 µmol/l (3–17)
ALT	25 IU/l (<40)
ALP	55 IU/l (40–130)
GGT	25 IU/l (10–50)
Albumin	39 g/l (35–50)
Morning urine	Haemoglobin and haemosiderin present

What is the most likely diagnosis?

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ALP	55 IU/l (40–130)
GGT	25 IU/l (10–50)
Albumin	39 g/l (35–50)
Morning urine	Haemoglobin and haemosiderin present

What is the most likely diagnosis?

A	Chronic lymphocytic leukaemia
B	Bladder cancer
C	Paroxysmal nocturnal haemoglobinuria
D	Glucose-6-phosphate dehydrogenase deficiency
E	Acute liver failure

71124

C Paroxysmal nocturnal haemoglobinuria

This patient has evidence of intravascular haemolysis – low haptoglobins, haemoglobin and haemosiderin in the urine and a raised bilirubin. If tested, his LDH would also be raised. This haemolysis has resulted in anaemia. He has also had a recent thrombosis in a rare location. He describes dark urine, which could be associated with any haemolytic disorder; however, the fact that the dark urine occurs in the morning, in the context of haemolysis and unusual thrombosis, points towards paroxysmal nocturnal haemoglobinuria (PNH).

PNH is a very rare acquired disorder associated with glycophosphatidylinositol deficiency, which results in the absence of certain red cell membrane proteins, namely CD55 and CD59. This leaves the cells prone to haemolysis, resulting in the

CD55 and CD59. This leaves the cells prone to haemolysis, resulting in the classical early morning 'Coca-Cola'-coloured urine (as this is when the urine is most concentrated). It is also associated with thrombosis, particularly in unusual locations such as the portal vein, mesenteric veins or hepatic vein (Budd–Chiari syndrome).

Diagnostic investigations would include flow cytometry to identify the absence of CD55 and CD59 on the red cell surface. Bone marrow aspiration and trephine is useful to classify PNH (i.e. in the absence or in the setting of another bone marrow disorder). The Ham test, looking at red cell fragility in acid, is no longer used due to its low specificity. Referral to the Haematology Registrar would be the most appropriate first step.

A	Chronic lymphocytic leukaemia

Chronic lymphocytic leukaemia (CLL) would be associated with a low

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A 55-year-old gentleman complained of a 2-month history of lower back pain. He had been feeling increasingly tired over the last few months and had noted weight loss of 1 stone. He had also noted some tingling in his hands and feet.

On examination, he was found to have gynaecomastia, a palpable 2 cm liver edge and peripheral oedema. There was evidence of loss of pinprick and joint position sense to the mid-shins bilaterally, and diffuse hyperpigmentation of the extremities.

Investigations:

Hb	9.6 g/dl
WCC	5.4 × 109/l
PLT	130 × 109/l
MCV	86 fl
Total protein	95 g/l
Albumin	30 g/l
Fasting Glucose	11 mmol/l

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Fasting Glucose	11 mmol/l
Thyrotropin	7.5 mU/l (0.5–5.5 mU/l)
Thyroxine (total free)	50 nmol/l (75–150 nmol/l)

What diagnosis best explains the patient's presentation?

A	Non Hodgkin's lymphoma
B	Waldenstrom's macroglobulinaemia
C	Classical multiple myeloma
D	Polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy and skin changes syndrome (POEMS)
E	Chronic lymphocytic leukaemia

Question 32 of 104

D Polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy and skin changes syndrome (POEMS)

POEMS syndrome is a rare multi-system disease that occurs in the setting of plasma cell dyscrasia. The pathophysiology of the disease is not known; however, elevated levels of cytokines and growth factors have been implicated.

The polyneuropathy associated with POEMS syndrome is a bilateral symmetric disturbance. It involves both motor and sensory nerves, begins distally and has a progressive proximal spread. Associated cranial or autonomic nerves are not involved. Both demyelination and axonal degeneration are noted. The liver, the lymph nodes, and the spleen are the organs most frequently involved.

Multiple endocrinopathies have been associated with POEMS syndrome, and

associated with POEMS syndrome, and most patients have more than one endocrine abnormality. POEMS syndrome is seen in the setting of a plasma cell dyscrasia. Although many plasma cell disorders have been reported in patients with POEMS syndrome, most patients are seen with osteosclerotic myeloma or monoclonal gammopathy of unknown significance (MGUS). Classic multiple myeloma is not usually associated with the disease.

A Non Hodgkin’s lymphoma

Most patients present with lymphadenopathy. Intermediate- or high-grade lymphomas can also be accompanied by beta symptoms (weight loss, temperature >38 °C, night sweats).

B Waldenstrom’s macroglobulinaemia

This is usually accompanied by

This usually presents with bone pain, pathological fractures, weakness, anaemia, infection (often pneumococcal), hypercalcaemia, spinal cord compression or kidney disease. It can also be accompanied by hyperviscosity syndrome (mucosal bleeding, visual changes and neurological symptoms).

E	Chronic lymphocytic leukaemia

Patients with chronic lymphocytic leukaemia (chronic lymphoid leukaemia, CLL) present with a wide range of symptoms and signs. Onset is insidious, and it is not unusual for CLL to be discovered incidentally after a blood cell count is performed for another reason; 25–50% of patients will be asymptomatic at time of presentation.

Other signs include lymphadenopathy, hepatospenomegaly, petechiae due to low platelet count, and pallor due to anaemia.

A 50-year-old man presents with fatigue. Two years ago, the patient received six cycles of combination therapy (each cycle consisted of cyclophosphamide, doxorubicin, vincristine and prednisolone) for non-Hodgkin's lymphoma in chest and abdominal sites.

The patient entered complete remission and has been followed expectantly since that point. His last visit was 3 months ago, at which time he had no evidence of recurrent lymphoma, felt well and had normal laboratory examination.

This time, his physical examination is remarkable for a purple discoloration of the fingertips, ears and nose. The patient is somewhat pale. There is no peripheral lymphadenopathy.

WCC	10×10^9/l (Neutrophils 7, lymphocytes 1, eosinophils 0.3, basophils 0.1, metamyelocytes 0.2, myelocytes 0.1 and nucleated red cells 0.1)

Haematocrit	28%
Hb	8.7 g/dl
Platelets	300×10^9/l
MCV	98 fl
LDH	400 U/l
Total bilirubin	51µmol/l (1–22)
Conjugated bilirubin	0.5 µmol/l (0–0.4)
Peripheral blood smear	Clumped cells
Polyspecific sera	+ for complement components

Which of the following is most likely to be expected on further testing?

A	Positive direct Coombs' test (using anti-IgG antiserum) if the specimen is processed without allowing cooling

Which of the following is most likely to be expected on further testing?

A	Positive direct Coombs' test (using anti-IgG antiserum) if the specimen is processed without allowing cooling
B	Positive indirect Coombs' test detected with anti-IgG antibodies
C	Circulating antibodies against Epstein-Barr virus
D	Circulating antibodies against red cells bearing the I antigen
E	Circulating antibodies against *Mycoplasma pneumoniae*

7709

remarkable for a purple discoloration of the fingertips, ears and nose. The patient is somewhat pale. There is no peripheral lymphadenopathy.

WCC	10×10^9/l (Neutrophils 7, lymphocytes 1, eosinophils 0.3, basophils 0.1, metamyelocytes 0.2, myelocytes 0.1 and nucleated red cells 0.1)
Haematocrit	28%
Hb	8.7 g/dl
Platelets	300×10^9/l
MCV	98 fl
LDH	400 U/l
Total bilirubin	51µmol/l (1–22)
Conjugated bilirubin	0.5 µmol/l (0–0.4)
Peripheral blood smear	Clumped cells

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D	Circulating antibodies against red cells bearing the I antigen

This patient has cold-reactive haemolysis or cold agglutinin disease. If patients develop circulating anti-IgM antibodies with specificity for polysaccharide antigens on red cell membranes, they may suffer from so-called ‘cold-reactive haemolysis’. The clinical manifestations of presence of such antibodies are haemolysis, which is generally not severe and a mild elevation of the reticulocyte count, agglutination of red cells, and an increased rate of haemolysis at temperatures below 37°C. A second clinical manifestation of cold haemolysis is the presence of acrocyanosis, characterized by marked purple discoloration of the extremities, ears and nose during cooling. IgM antibodies may be missed if the blood is allowed to cool after it is drawn because of absorption onto the patient’s own red blood cells and subsequent removal as the blood clots. Therefore, the blood should be allowed

to clot at a warm temperature. Serological analysis will reveal a positive direct Coombs' test if anti-C3 antiserum is used. The specificity of cold agglutinin antibody may be helpful in that a reaction with adult red cells compared with fetal blood is more common in benign lymphoproliferative disorders. On the other hand, antibodies that react more strongly with fetal cells compared with adult red cells are called anti-i and are generally seen in lymphomas and in infectious mononucleosis. This patient may well have recurrence of his lymphoma, which is presenting as cold haemolytic disease because of the presence of monoclonal IgM antibody. The problem is best treated with anti-lymphoma therapy.

B	Positive indirect Coombs' test detected with anti-IgG antibodies

Indirect Coombs' testing is mainly used in cross-matching for blood transfusions or prenatal testing for

transfusions or prenatal testing for serum IgG antibodies that may cross the placenta and cause haemolytic disease of the newborn.

A	Positive direct Coombs' test (using anti-IgG antiserum) if the specimen is processed without allowing cooling

A direct Coombs' test will be only positive with anti-C3 serum for cold reactive haemolysis, because the auto-antibody is IgG-complement based and, in cold temperatures, IgG causes complement to irreversibly bind to red blood cells.

C	Circulating antibodies against Epstein–Barr virus

EBV can cause autoimmune haemolysis. IgG antibodies to EBV show a previous infection, a positive IgM antibodies show a current infection. Complement components would not be positive in this case.

EBV can cause autoimmune haemolysis. IgG antibodies to EBV show a previous infection, a positive IgM antibodies show a current infection. Complement components would not be positive in this case. Blood film in EBV would show 50% lymphocytes and 10% atypical lymphocytes.

E	Circulating antibodies against *Mycoplasma pneumoniae*

Gold standard testing for mycoplasma pneumoniae is having two positive IgM or IgG results 2-4 weeks apart, as a single positive may be the result of a recent previous infection and some people do not mount an immune response. Patients usually have non-specific flu-like or cold-like symptoms. Many patients will have a leucocytosis and some have a raised ESR.

7709

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A 65-year-old man is admitted with dehydration following an attack of infectious gastritis.

His initial blood results revealed a raised calcium and erythrocyte sedimentation rate. He has a background of hypertension, angina, chronic obstructive airways disease and diabetes.

His most recent results arrive on the ward:

Hb	13.8 g/dl
WCC	7.7 × 10^9/l
PLT	212 × 10^9/l
Na^+	138 mmol/l
K^+	4.7 mmol/l
Creatinine	104 µmol/l
Urea	7.2 mmol/l
Ca^{2+}	2.4 mmol/l
Albumin	38 g/l
	19 g/l (6.0–13.0,

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IgG	19 g/l (6.0–13.0, monoclonal band identified)
IgA	2.1 g/l (0.8–3.0)
IgM	1.3 g/l (0.4–2.5)
Urine, Bence Jones protein	-
Chest X-ray	Heart and mediastinal contours normal, lungs clear, osteopenia of bony skeleton with no lytic lesions

What is the most likely diagnosis?

A	Monoclonal gammopathy of undetermined significance
B	Multiple myeloma
C	Waldenström’s macroglobulinaemia

protein	
Chest X-ray	Heart and mediastinal contours normal, lungs clear, osteopenia of bony skeleton with no lytic lesions

What is the most likely diagnosis?

A	Monoclonal gammopathy of undetermined significance
B	Multiple myeloma
C	Waldenström's macroglobulinaemia
D	Inflammatory amyloidosis
E	Chronic lymphocytic leukaemia

7079

Albumin	38 g/l
IgG	19 g/l (6.0–13.0, monoclonal band identified)
IgA	2.1 g/l (0.8–3.0)
IgM	1.3 g/l (0.4–2.5)
Urine, Bence Jones protein	-
Chest X-ray	Heart and mediastinal contours normal, lungs clear, osteopenia of bony skeleton with no lytic lesions

What is the most likely diagnosis?

Your answer was correct

A Monoclonal gammopathy of undetermined significance

A Monoclonal gammopathy of undetermined significance

monoclonal gammopathy of undetermined significance (MGUS), which is a monoclonal paraproteinaemia without evidence of disorders such as myeloma, Waldenström's macroglobulinaemia or amyloidosis. It is usually picked up incidentally. There is mild increase in a serum monoclonal protein without paresis of the other monoclonal bands. The presence of anaemia, hypercalcaemia, kidney disease or lytic bone lesions points towards myeloma. The initial raised calcium is most likely to have been related to dehydration. In MGUS the urine does not contain Bence Jones protein. These patients need to be followed up as they are at increased risk of developing myeloma. A bone marrow biopsy should reveal <10% plasma cells and a skeletal survey should reveal no lytic lesions to be compatible with MGUS.

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B Multiple myeloma

Multiple myeloma is associated with evidence of end-organ damage, where for example elevated creatinine would be expected. A greater increase in the monoclonal gammopathy may also be expected.

C Waldenström's macroglobulinaemia

Waldenström's macroglobulinaemia is associated with elevated IgM and with hyperviscosity rather than the features seen here.

D Inflammatory amyloidosis

In inflammatory amyloidosis a polyclonal increase in immunoglobulins would be expected against a background of chronic inflammatory disease.

E Chronic lymphocytic leukaemia

A 38-year-old woman, who had a deep vein thrombosis (DVT) during pregnancy 10 years previously, attends her general practitioner (GP) as she is due to fly to Australia and has been reading in the newspapers about 'traveller's thrombosis' and 'economy class syndrome'.

She is not currently on any medication, except for the combined oral contraceptive pill; she has a past medical history of fibromyalgia and irritable bowel syndrome, smokes 20 cigarettes per day and drinks 20 units of alcohol per week.

The GP performs a thrombophilia screen, shown below:

Protein C	90 iu/dl (80–135)
Protein S	85 iu/dl (80–120)
Antithrombin III	80 iu/dl (80–120)
Activated protein C resistance	3.2 (2.12–4.0)

	120)
Activated protein C resistance	3.2 (2.12–4.0)
D-dimer	0.3 mg/l (< 0.5 mg/l)

The GP then contacts you with the results, and asks what he should give her for her journey.

What management do you recommend for this patient?

A	Aspirin
B	Warfarin
C	Low-molecular weight heparin
D	Regular ankle and calf exercises only
E	Graduated compression stockings

Question 3 of 73

A 38-year-old woman, who had a deep vein thrombosis (DVT) during pregnancy 10 years previously, attends her general practitioner (GP) as she is due to fly to Australia and has been reading in the newspapers about ‘traveller’s thrombosis’ and ‘economy class syndrome’.

She is not currently on any medication, except for the combined oral contraceptive pill; she has a past medical history of fibromyalgia and irritable bowel syndrome, smokes 20 cigarettes per day and drinks 20 units of alcohol per week.

The GP performs a thrombophilia screen, shown below:

Protein C	90 iu/dl (80–135)
Protein S	85 iu/dl (80–120)
Antithrombin III	80 iu/dl (80–120)
Activated protein C	

E Graduated compression stockings

There has recently been considerable media interest in the risk of blood clots triggered by air flights. A study from North America indicated that the risk of a fatal blood clot after a transatlantic flight is < 1 in a million. Additional studies indicate that the greatest risk of a blood clot is when there are additional risk factors such as surgery in the previous few weeks. The risk is related to the duration of travel, with the lowest risk for journeys of < 6 h. This particular patient has a moderate risk for DVT, as she had a DVT in the past. She is also on an oral contraceptive and smokes cigarettes, both of which increase her risk from low to moderate.

Classification of risk category and suggested precautions for continuous journeys lasting > 6 h are as follows:

Low risk:

- no history of DVT or pulmonary

Low risk:

- no history of DVT or pulmonary embolism (PE)
- no surgery in the previous 4 weeks
- no other risk factors.

Recommendations:

- Do not take excessive alcohol or sleeping tablets.
- Regularly flex the ankles to contract the calf muscles.

Moderate risk:

- previous history of DVT (or PE)
- surgery under general anaesthesia (GA) lasting > 30 minutes in the previous 2 months but not in the last 4 weeks
- pregnant or postpartum
- cardiac disease or other major acute illness (eg pneumonia)

acute illness (eg pneumonia)
- oral contraceptives or hormone replacement therapy
- obesity
- family history of first-degree relative with VTE
- polycythaemia
- lower limb fracture in a plaster cast.

Recommendations:

- Do not take excessive alcohol or sleeping tablets.
- Regularly flex the ankles to contract the calf muscles.
- Wear graduated compression travel stockings.

High risk:

- surgery under GA lasting > 30 minutes in the previous 4 weeks
- active cancer
- known thrombophilia

High risk:

- surgery under GA lasting > 30 minutes in the previous 4 weeks
- active cancer
- known thrombophilia.

Recommendations:

- Assess suitability for long-haul flights.
- Do not take excessive alcohol or sleeping tablets.
- Regularly flex the ankles to contract the calf muscles.
- Wear graduated compression travel stockings.
- Consider a single injection of LMWH before departure, and ensure there is enough for the flight back.

D	Regular ankle and calf

D Regular ankle and calf exercises only

This is recommended for patients who are low risk. This patient is moderate risk and is recommended to do the ankle and calf exercises regularly, as well as wearing graduated compression stockings. Calf and ankle exercises should be undertaken by all people travelling on long-haul flights, in addition to other recommendations by their medical doctor.

A Aspirin

Aspirin is not recommended as venous thromboembolism (VTE) treatment or prophylaxis. There is controversial evidence available for the use of aspirin in VTE prevention. There have been a few studies that showed it is not inferior to low-molecular-weight heparin (LMWH) for post-operative orthopaedic patients. In the case of this patient, however, she is moderate risk, and therefore, drug treatment is

Question 3 of 73

heparin (LMWH) for post-operative orthopaedic patients. In the case of this patient, however, she is moderate risk, and therefore, drug treatment is not recommended.

B	Warfarin

Warfarin is used in the case of established VTE, and not as prevention. Regardless, in the case of this patient, however, she is moderate risk, and therefore, drug treatment is not recommended.

C	Low-molecular weight heparin

LMWH is used as a one-off dose pre-flight for patients who have a high risk for developing VTE. This patient is moderate risk and therefore does not require LMWH.

8546

Rate this question: ⊖ ★★★★★

An 18-year-old single man is referred who suffers recurrent oesophageal candidiasis. He has a background medical history of asthma treated with inhaled steroids and eczema.

Labs show no B cells and reduced immunoglobulins, CD4 T-lymphocyte count is normal and platelet count is reduced.

What diagnosis fits best with this clinical picture?

A	Chronic myeloid leukaemia
B	HIV infection
C	Inappropriate inhaler use
D	Infectious mononucleosis
E	Primary immunodeficiency

71098

An 18-year-old single man is referred who suffers recurrent oesophageal candidiasis. He has a background medical history of asthma treated with inhaled steroids and eczema.

Labs show no B cells and reduced immunoglobulins, CD4 T-lymphocyte count is normal and platelet count is reduced.

What diagnosis fits best with this clinical picture?

Your answer was correct

A Chronic myeloid leukaemia

B HIV infection

C Inappropriate inhaler use

D Infectious mononucleosis

E Primary immunodeficiency

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E	Primary immunodeficiency

Wiskott–Aldrich syndrome is an X-linked disorder associated with eczema and thrombocytopenia, associated with reduced levels of immunoglobulins. Patients often suffer from associated autoimmune disorders and are at increased risk of lymphoreticular malignancy.

A	Chronic myeloid leukaemia

CML has a tri- or biphasic clinical course: a chronic phase, which is present at the time of diagnosis in approximately 85% of patients; an accelerated phase, in which neutrophil differentiation becomes progressively impaired and leukocyte counts are more difficult to control with treatment; and blast crisis, a condition resembling acute leukaemia in which myeloid or lymphoid blasts proliferate in an uncontrolled manner. The peripheral smear typically demonstrates a leukocytosis with a median white count of approximately

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median white count of approximately 10 × 109 mmol/l. The WBC differential typically shows virtually all cells of the neutrophilic series, from myeloblasts to mature neutrophils with peaks in the percentages of myelocytes and segmented neutrophils. Blasts typically account for <2%. The presence of a greater percentage of myelocytes than the more mature metamyelocytes (‘leukemic hiatus’ or ‘myelocyte bulge’) is one of the classic findings in CML. The granulocytes of the chronic phase are morphologically normal with no evidence of dysplasia, but dysplasia can develop in more advanced disease, and particularly in the accelerated phase. The blood picture in this scenario is not consistent with CML.

B	HIV infection

The normal CD4 count makes AIDS less likely as the cause in this case.

C	Inappropriate inhaler use

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C Inappropriate inhaler use

Inappropriate inhaler use will not provide an explanation for the blood picture here.

D Infectious mononucleosis

Infectious mononucleosis (IM) is characterised by a triad of fever, tonsillar pharyngitis and lymphadenopathy. The most common laboratory finding in association with infectious mononucleosis (IM) is lymphocytosis, defined as an absolute count >4500/microl or, on peripheral smear, a differential count >50%. The smear may also identify significant atypical lymphocytosis, defined as >10% of total lymphocytes. The majority of reactive lymphocytes in patients with IM are CD8+ cytotoxic T cells. In one study, the severity of illness correlated with the magnitude of CD8+ lymphocytosis (as well as with blood Epstein-Barr viral (EBV) load). The blood picture in this scenario is not consistent with IM.

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A 24-year-old woman presented to the Emergency Department with an 18 h history of a severe headache, right-sided hemiparesis and new-onset grand mal seizures. She denied taking any medication or recreational drugs.

She had a temperature of 37.6 °C, pulse 120 bpm, sinus rhythm and a blood pressure of 110/80 mmHg.

Investigations:

Hb	6.4 g/dl
WCC	10.0 × 10^9/l
PLT	10.0 × 10^9/l
INR	1.3
APTT	26 s (25–41)
Creatinine	150 μmol/l
Urea	10.0 mmol/l
Bilirubin	90 μmol/l
AST	21 U/l
ALT	25 U/l

Bilirubin	90 µmol/l
AST	21 U/l
ALT	25 U/l
LDH	3200 U/l

What is the most likely unifying diagnosis?

A	Idiopathic thrombocytopenic purpura
B	Disseminated intravascular coagulation
C	Thrombotic thrombocytopenic purpura
D	Haemolytic uraemic syndrome
E	Cocaine abuse

C Thrombotic thrombocytopenic purpura

Thrombotic thrombocytopenic purpura (TTP) is a life-threatening multi-system disorder characterised by micro-angiopathic haemolytic anaemia, thrombocytopenia, neurological abnormalities, fever and renal dysfunction. With the introduction of plasma exchange, the survival rate has improved from approximately 3% prior to the 1960s to 82% now. Platelet transfusions are contraindicated. Fresh-frozen plasma, methylprednisolone and red cell support are all important additional supportive measures.

A Idiopathic thrombocytopenic purpura

Idiopathic thrombocytopenic purpura (ITP), also known as primary immune thrombocytopenic purpura and autoimmune thrombocytopenic purpura, is defined as isolated thrombocytopenia with normal bone

thrombocytopenia with normal bone marrow in the absence of other causes of thrombocytopenia.

B	Disseminated intravascular coagulation

Disseminated intravascular coagulation (DIC) is a complex systemic thrombo-haemorrhagic disorder involving the generation of intravascular fibrin and the consumption of procoagulants and platelets. It is seen in association with a number of well-defined clinical situations, including sepsis, major trauma and abruptio placenta. It is associated with prolonged clotting times, low fibrinogen, raised fibrin degradation products and thrombocytopenia.

D	Haemolytic uraemic syndrome

Haemolytic uraemic syndrome (HUS) is characterised by acute kidney disease, micro-angiopathic haemolytic anaemia, fever and thrombocytopenia

E Cocaine abuse

Cocaine is a complex drug that can cause lethal cardiovascular events, including myocardial infarction and ventricular arrhythmias. The exact mechanism of cocaine-related stroke remains unclear, and there are likely to be a number of factors involved. There does not appear to be any direct neurotoxic action, and potential mechanisms involved in cocaine induced stroke include vasospasm, cerebral vasculitis, enhanced platelet aggregation, cardio-embolism and hypertensive surges associated with altered cerebral autoregulation and cerebral blood flow. Cocaine use is associated with both intracerebral haemorrhage and subarachnoid haemorrhage. As with ischaemic stroke, the exact mechanism involved is not fully understood, though may involve cocaine-induced haemodynamic changes in susceptible individuals

A 35-year-old alcoholic is admitted after an upper GI haemorrhage. An endoscopy is performed soon after admission with variceal banding, but you are asked to see him the following morning as he is drowsy and confused.

On examination, his BP is 100/60 mmHg, pulse is 75/min and regular and his temperature is 36.5°C. He is mildly tender in the epigastrium and there is evidence of ascites. He is very drowsy and appears confused when you wake him from sleep. PR reveals melaena.

Investigations:

Hb	9.1 g/dl
WCC	10.5 x 10^9/l
PLT	131 x 10^9/l
Na^+	128 mmol/l
K^+	5.1 mmol/l
Creatinine	122 micromol/l
CRP	17 mg/l
Albumin	23 g/l

Creatinine	122 micromol/l
CRP	17 mg/l
Albumin	23 g/l
ALT	231 U/l
Glucose	5.9 mmol/l

Which of the following is most likely to reveal the cause of his confusion?

A Serum ammonia

B Ascitic tap

C Blood cultures

D CT head

E Lumbar puncture

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A Serum ammonia

The fact that the increased confusion has occurred following the upper GI bleed is suggestive that blood ingestion has led to increased ammonia production by the bacteria within the GI tract. Strategies to reduce bacterial ammonia production include use of neomycin and lactulose.

B Ascitic tap

Spontaneous bacterial peritonitis is potentially one of the differential diagnoses in a case of confusion in a patient with decompensated alcoholic liver disease; in the current situation, however, the onset of confusion soon after the GI bleed points towards the blood ingestion and ammonia production as the likeliest cause.

C Blood cultures

Sepsis is a potential cause of confusion, but in this scenario there is

10:25

Question 6 of 73

C	Blood cultures

Sepsis is a potential cause of confusion, but in this scenario there is no evidence for it, either from the physical examination/observations or from the blood results.

D	CT head

A subdural haematoma could be another cause for confusion, but in our case there is no history of fall or head injury.

E	Lumbar puncture

Neither the history nor the blood results support the diagnosis of meningitis/encephalitis.

37191

Rate this question:

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You are called urgently to see a 60-year-old man with an acute blood transfusion reaction. The patient had a total hip replacement the previous day and had just started a routine blood transfusion when he complained of feeling faint and breathless.

Examination shows an unwell, breathless man: pulse 120 bpm, blood pressure 70 mmHg systolic, respiratory rate 35 breaths/min, temperature 38.9 °C, Glasgow Coma Scale (GCS) score 13/15. There is widespread wheeze on auscultation of the chest. The patient's blood group is group A rhesus-negative; the blood transfusion is group O rhesus-negative.

What is the most likely cause of this patient's deterioration?

A	Bacterial contamination of the unit of blood
B	Transfusion related acute lung injury (TRALI)

blood group is group A rhesus-negative; the blood transfusion is group O rhesus-negative.

What is the most likely cause of this patient's deterioration?

A	Bacterial contamination of the unit of blood
B	Transfusion related acute lung injury (TRALI)
C	Acute intravascular haemolysis due to inappropriate ABO crossmatching
D	Acute transfusion reaction due to donor cytokines
E	Acute intravascular haemolysis due to inappropriate Kell crossmatching

total hip replacement the previous day and had just started a routine blood transfusion when he complained of feeling faint and breathless.

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What is the most likely cause of this patient's deterioration?

Your answer was incorrect

A	Bacterial contamination of the unit of blood
B	Transfusion related acute lung injury (TRALI)
C	Acute intravascular

🟩 **A** Bacterial contamination of the unit of blood

Bacterial contamination is a possibility, although this is very rare with red cell transfusions and more common with platelet transfusions (which are stored at room temperature). However, if such contaminated blood is stored for a few days at room temperature (eg platelets) or for a few weeks at refrigerated temperature (eg red cells), bacteria may grow and elaborate endotoxin, which is a major adverse factor in such reactions and drives the acute presentation seen here.

🟥 **D** Acute transfusion reaction due to donor cytokines

When patients donate blood at the time of viral infection, increased levels of inflammatory cytokines may be present in the donated unit. These usually cause mild pyrexia, rather than the acute symptoms seen here.

TRALI is associated with acute-onset non-cardiogenic pulmonary oedema; it is thought to be related to donor antibodies to human leukocyte antigens, which drive neutrophil activation.

C	Acute intravascular haemolysis due to inappropriate ABO crossmatching

Immunoglobulin M (IgM) anti-A and anti-B antibodies cause acute haemolytic transfusion reactions, and as little as 4 ml of transfused ABO-incompatible blood can be fatal. As far as we are aware, the labelling of the blood as O rhesus-negative means that an acute transfusion reaction should not be seen.

E	Acute intravascular haemolysis due to inappropriate Kell crossmatching

immunoglobulin M (IgM) anti-A and anti-B antibodies cause acute haemolytic transfusion reactions, and as little as 4 ml of transfused ABO-incompatible blood can be fatal. As far as we are aware, the labelling of the blood as O rhesus-negative means that an acute transfusion reaction should not be seen.

E	Acute intravascular haemolysis due to inappropriate Kell crossmatching

Delayed haemolytic transfusion reactions are more likely to be seen in patients with inappropriate Kell crossmatching, rather than the acute presentation seen here. In addition, Kell positivity is relatively rare in the Caucasian population (approximately 9%) and is done as part of a standard crossmatch panel.

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A 28-year-old woman is brought to the Emergency Department by her husband. She has had a fever and abdominal pain for four days and has been complaining of a headache for the past 24 h. Her husband tells you that they visited a hobby / petting farm with their two children a few days earlier.

On examination, she is restless and has a temperature of 38 °C, pallor and a purpuric rash on her legs and abdomen. There is no nuchal rigidity. Her blood pressure is 150/90 mmHg. The rest of the examination is normal.

Investigations:

Hb	8.7 g/dl
WCC	11.0×10^9/l
PLT	10.0×10^9/l
D-dimer	-
Urea	8.4 mmol/l
Creatinine	150 µmol/l

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Lactate dehydrogenase (LDH)	2160 IU/l (200–450)
Antinuclear antibody (ANA)	-
Direct agglutination test (DAT)	-
Peripheral smear	Anisocytosis, poikilocytosis, frequent schistocytes and polychromasia, marked thrombocytopenia, leukocytes normal
Urinalysis	Trace protein

A CT scan of the brain and an abdominal ultrasound scan are both normal. Lumbar puncture is not performed because of the thrombocytopenia.

Which one of the following diagnoses

Urinalysis	Trace protein

A CT scan of the brain and an abdominal ultrasound scan are both normal. Lumbar puncture is not performed because of the thrombocytopenia.

Which one of the following diagnoses best fits the above picture?

A	Evans syndrome
B	Systemic lupus erythematosus (SLE)
C	Thrombotic thrombocytopenic purpura (TTP)
D	Meningococcal meningitis
E	Metastatic cancer

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C | Thrombotic thrombocytopenic purpura (TTP)

A high index of suspicion is necessary to make this diagnosis, and the visit to a farm raises the possibility of *E coli* infection, recognised as a cause of TTP. Although characterised by the pentad of fever, micro-angiopathic haemolytic anaemia (MAHA), thrombocytopenia, neurological abnormalities and kidney disease, in practice the triad of schistocytes, thrombocytopenia and an elevated LDH are sufficient to make the diagnosis. Coagulation tests are normal and there is no evidence of disseminated intravascular coagulation (DIC). The introduction of daily plasma exchange has transformed the prognosis of this previously fatal disorder. Pathologically, widespread platelet microthrombi are evident. These result from aggregates of platelets and circulating ultra-high-molecular weight von Willebrand factor (vWF) multimers; the latter are normally cleaved by a circulating

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normally cleaved by a circulating metalloprotease, ADAMTS 13. This enzyme is deficient in TTP. Plasmapheresis is thought to replace this enzyme, and also may aid in the removal of large vWF multimers..

A	Evans syndrome

This autoimmune disorder with unknown pathophysiology is characterised by the simultaneous or sequential co-existence of autoimmune haemolytic anaemia with immune-mediated thrombocytopenia.

B	Systemic lupus erythematosus (SLE)

This is an autoimmune disorder and the antinuclear antibody test is positive. Other features including joint pains and a photosensitive rash are also absent.

D	Meningococcal meningitis

B Systemic lupus erythematosus (SLE)

This is an autoimmune disorder and the antinuclear antibody test is positive. Other features including joint pains and a photosensitive rash are also absent.

D Meningococcal meningitis

This is the main differential, although the visit to a hobby farm makes us more suspicious of TTP as the underlying cause of her symptoms.

E Metastatic cancer

The normal CT brain and ultrasound of the abdomen make this much less likely.

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A 72-year-old patient is treated with warfarin for a prosthetic aortic valve. He has completed a 5-day course of oral ciprofloxacin for a sinus infection, and he is attending for an international normalised ratio (INR) check. There is no increase in bruising or bleeding from mucus membranes.

Investigations:

Hb	12.5 g/dl
WCC	7.1 x 10^9/l
PLT	203 x 10^9/l
Na^+	139 mmol/l
K^+	4.4 mmol/l
Creatinine	129 µmol/l
INR	6.8

Which of the following is the most appropriate management with respect to his INR?

A	Stop warfarin and review INR in 24 hours

Na^+	139 mmol/l
K^+	4.4 mmol/l
Creatinine	129 µmol/l
INR	6.8

Which of the following is the most appropriate management with respect to his INR?

A Stop warfarin and review INR in 24 hours

B Give 10 mg IV vitamin K

C Give fresh frozen plasma (FFP)

D Give prothrombin complex concentrate

E Give dextran sulphate

23325

A 72-year-old patient is treated with warfarin for a prosthetic aortic valve. He has completed a 5-day course of oral ciprofloxacin for a sinus infection, and he is attending for an international normalised ratio (INR) check. There is no increase in bruising or bleeding from mucus membranes.

Investigations:

Hb	12.5 g/dl
WCC	7.1 x 10^9/l
PLT	203 x 10^9/l
Na^+	139 mmol/l
K^+	4.4 mmol/l
Creatinine	129 µmol/l
INR	6.8

Which of the following is the most appropriate management with respect to his INR?

Your answer was incorrect

A Stop warfarin and review INR in 24 hours

This man has an artificial valve and, as such, must maintain his INR around 3.0. He is not actively bleeding and therefore the most appropriate management is to allow his INR to drift down slowly over the next few days. Given that over-reversal of anticoagulation may be associated with significant embolic risk, dose omission in the absence of active bleeding is the safest option.

B Give 10 mg IV vitamin K

This risks over-reversal of the elevated INR and arterial embolism related to the prosthetic aortic valve.

C Give fresh frozen plasma (FFP)

FFP or other warfarin reversal agents, such as prothrombin complex concentrate, should only be

FFP or other warfarin reversal agents, such as prothrombin complex concentrate, should only be considered when there is life-threatening haemorrhage or surgery is urgently required.

D	Give prothrombin complex concentrate

PCC is considered when patients who have been taking warfarin need to progress urgently to surgery or have life-threatening haemorrhage.

E	Give dextran sulphate

Dextran sulphate is the reversal agent for over-heparinisation, and is not of value in treating excessive warfarinisation.

23325

A 58-year-old woman is admitted for resection of a caecal carcinoma. She is not taking any medications, has no other past medical history, is a non-smoker and drinks little alcohol. Preoperative physical examination is unremarkable, with a blood pressure of 125/85 mmHg, pulse 76/min and regular. BMI is 23.

Preoperative bloods:

Hb	9.0 g/dl
MCV	76 fl
WCC	10.0×10^9/l
PLT	250×10^9/l

The operation was uneventful. with no evidence of secondary spread and the patient received 2 units of blood during the procedure. Five days later she was icteric and tired. She is apyrexial, and apart from tenderness around her scar, she tells you that her surgical pain is gradually improving.

Repeat bloods:

Question 10 of 73

Repeat bloods:

Hb	6.0 g/dl
WCC	15.0 × 10^9/l
PLT	450 × 10^9/l
MCV	100 fl
Bilirubin	80 µmol/l
AST	30 IU/l
ALP	100 IU/l
Blood film	Polychromasia, spherocytes

Which investigation will most likely lead to a confirmed diagnosis?

A	Anti-cardiolipin antibodies
B	Serum haptoglobin
C	Reticulocyte count
D	Abdominal ultrasound scan

Question 10 of 73

MCV	100 fl
Bilirubin	80 µmol/l
AST	30 IU/l
ALP	100 IU/l
Blood film	Polychromasia, spherocytes

Which investigation will most likely lead to a confirmed diagnosis?

A Anti-cardiolipin antibodies

B Serum haptoglobin

C Reticulocyte count

D Abdominal ultrasound scan (USS)

E Direct antiglobulin test

9856

Question 10 of 73

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Repeat bloods:

Hb	6.0 g/dl
WCC	15.0 × 10^9/l
PLT	450 × 10^9/l
MCV	100 fl
Bilirubin	80 μmol/l
AST	30 IU/l
ALP	100 IU/l
Blood film	Polychromasia, spherocytes

Which investigation will most likely lead to a confirmed diagnosis?

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E	Direct antiglobulin test

Delayed transfusion reactions occur 5–10 days after transfusion and are almost invariably delayed haemolytic reactions due to the development of red cell (RBC) allo-antibodies. Clinical features are usually minimal but can include unexplained pyrexia, jaundice or unexplained drop in haemoglobin. Urinalysis shows urobilinogenuria and a blood shows fragile ballooned spherocytes. Diagnosis is confirmed by a direct antiglobulin (Coombs') test that detects the presence of antibody on the RBCs. The test is performed by adding anti-human globulin (AHG) (anti-Ig G and anti-complement) to the patient's washed RBCs. A positive test results in red cell agglutination.

A	Anti-cardiolipin antibodies

Anti-cardiolipin antibodies lead to prolongation of APTT and increased risk of thrombosis, rather than haemolysis.

prolongation of APTT and increased risk of thrombosis, rather than haemolysis.

B	Serum haptoglobin

Haptoglobin is decreased in conditions of haemolysis, although it does not confirm the underlying cause.

C	Reticulocyte count

Reticulocytes are elevated in patients with haemolysis, although they don’t indicate the underlying cause.

D	Abdominal ultrasound scan (USS)

Although blood loss as a result of the procedure may result in a haemoglobin of 60 g/l, the elevated bilirubin suggests that haemolysis as the more likely cause here.

9856

Rate this question: ⊖ ★★★★★

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A 71-year-old woman presents with tiredness and lethargy. Her GP had previously noted that she was anaemic and commenced iron therapy.

Examination reveals obvious splenic enlargement.

Investigations:

WCC	2.1 × 10^9 mmol/l
Neutrophils	0.9 × 10^9 mmol/l (1.5–7.0)
Lymphocytes	0.8 × 10^9 mmol/l (1.5–4.0)
Monocytes	0.1 × 10^9 mmol/l (0–0.8)
Eosinophils	0 × 10^9 mmol/l (0.04–0.4)
Basophils	0 × 10^9 mmol/l (0–0.1)
Hb	9.1 g/dl
MCV	80 fl (76–96)
PLT	90 × 10^9 mmol/l (150–400)

Hb	9.1 g/dl
MCV	80 fl (76–96)
PLT	90 × 10^9 mmol/l (150–400)

Bone marrow biopsy reveals increased cellularity.

What diagnosis fits best with this clinical picture?

A	Acute myeloid leukaemia (AML)
B	Chronic myeloid leukaemia
C	Myelodysplasia
D	Myelofibrosis
E	Myeloma

71096

Lymphocytes	0.8 × 10^9 mmol/l (1.5–4.0)
Monocytes	0.1 × 10^9 mmol/l (0–0.8)
Eosinophils	0 × 10^9 mmol/l (0.04–0.4)
Basophils	0 × 10^9 mmol/l (0–0.1)
Hb	9.1 g/dl
MCV	80 fl (76–96)
PLT	90 × 10^9 mmol/l (150–400)

Bone marrow biopsy reveals increased cellularity.

What diagnosis fits best with this clinical picture?

Your answer was correct

A	Acute myeloid leukaemia (AML)

C Myelodysplasia

Myelodysplasia occurs mainly in the elderly and presents with anaemia, infection or bleeding due to pancytopenia. Serial blood counts show evidence of increasing bone marrow failure and the bone marrow shows increased cellularity. Patients with <5% blasts in the bone marrow are managed conservatively, ‘gentle’ chemotherapy is used in patients with high WBC counts and intensive chemotherapy is usually reserved for patients under the age of 60 years. Transformation into AML occurs in around 30% of patients.

A Acute myeloid leukaemia (AML)

Patients with AML generally present with symptoms related to complications of pancytopenia (e.g. anaemia, neutropenia and thrombocytopenia), including weakness and easy fatigability, infections of variable severity and/or

infections of variable severity and/or haemorrhagic findings such as gingival bleeding, ecchymoses, epistaxis or menorrhagia. Bone marrow aspiration and biopsy (usually unilateral) is a key component in the diagnosis of AML. The bone marrow is usually hypercellular due to a partial or almost total replacement of the normal cellular components by immature or undifferentiated cells, although AML can sometimes present with a hypocellular marrow.

B	Chronic myeloid leukaemia

CML has a tri- or biphasic clinical course: a chronic phase, which is present at the time of diagnosis in approximately 85% of patients; an accelerated phase, in which neutrophil differentiation becomes progressively impaired and leukocyte counts are more difficult to control with treatment; and blast crisis, a condition resembling acute leukaemia in which myeloid or lymphoid blasts proliferate in an uncontrolled manner. The

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in an uncontrolled manner. The peripheral smear typically demonstrates a leukocytosis with a median WCC of approximately 10 × 10^9 mmol/l. The white blood cell differential typically shows virtually all cells of the neutrophilic series, from myeloblasts to mature neutrophils with peaks in the percentages of myelocytes and segmented neutrophils . Blasts typically account for <2%. The presence of a higher percentage of myelocytes than the more mature metamyelocytes (‘leukemic hiatus’ or ‘myelocyte bulge’) is one of the classic findings in CML. The granulocytes of the chronic phase are morphologically normal with no evidence of dysplasia, but dysplasia can develop in more advanced disease, and particularly in the accelerated phase.

D Myelofibrosis

Primary myelofibrosis (PMF) is one of the chronic myeloproliferative disorders, which are collectively characterised by clonal proliferation of

characterised by clonal proliferation of myeloid cells with variable morphologic maturity and haematopoietic efficiency. Splenomegaly is a marked feature. Bone marrow biopsy is necessary to demonstrate fibrosis. Some degree of fibrosis is seen in almost all patients; the fibrosis is typically extensive and is better visualised with a silver stain (reticulin) or a trichrome stain (mature collagen). Bone marrow sinusoids are expanded and there is intravascular haematopoiesis. The fibrosis is generally associated with atypical megakaryocytic hyperplasia, and thickening and distortion of the bony trabeculae (osteosclerosis).

E	Myeloma

Multiple myeloma (MM) is characterised by the neoplastic proliferation of plasma cells producing a monoclonal immunoglobulin. The plasma cells proliferate in the bone marrow, and this often results in extensive skeletal destruction with

osteolytic lesions, osteopenia and/or pathological fractures. The diagnosis of MM is often suspected because of one (or more) of the following clinical presentations: bone pain with lytic lesions discovered on routine skeletal films or other imaging modalities; an increased total serum protein concentration and/or the presence of a monoclonal protein in the urine or serum; systemic signs or symptoms suggestive of malignancy, such as unexplained anaemia, or hypercalcaemia, which is either symptomatic or discovered incidentally; acute kidney disease with a bland urinalysis; or, rarely, nephrotic syndrome due to concurrent immunoglobulin light-chain (AL) amyloidosis. The vast majority (97%) of patients with MM will have a monoclonal (M) protein produced and secreted by the malignant plasma cells, and this can be detected by protein electrophoresis of the serum and/or an aliquot of urine from a 24 h collection, combined with immunofixation of the serum and urine.

A 25-year-old woman is referred to the Haematology Clinic by her general practitioner (GP) after complaining of fatigue and breathlessness on exertion.

On examination, she is pale, with a spleen just palpable and no other abnormal findings.

The haemoglobin level is 9.6 g/dl.

Her blood film is shown below:

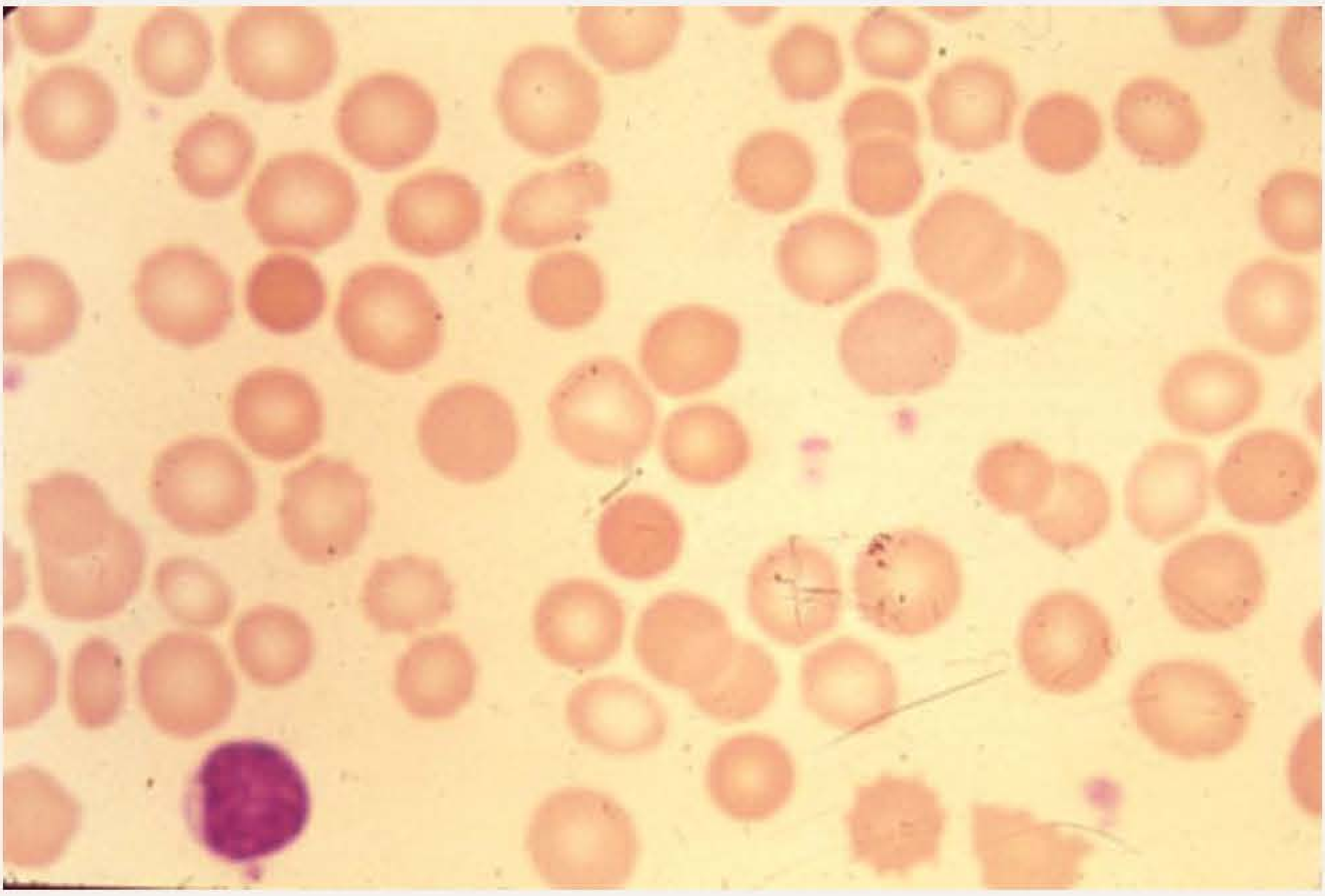

Image courtesy of the Crookston Collection, Toronto.

What is the most likely diagnosis?

A Hyposplenism

11:29

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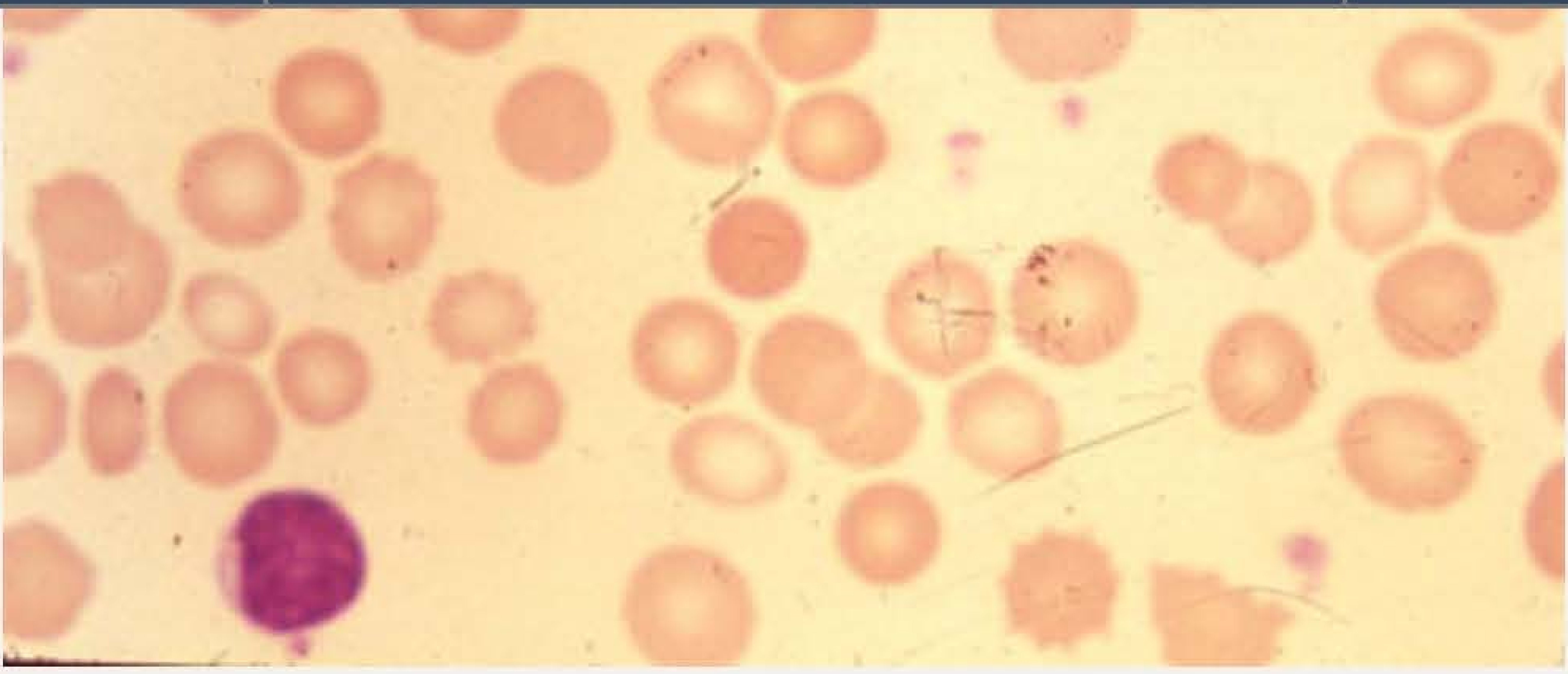

Image courtesy of the Crookston Collection, Toronto.

What is the most likely diagnosis?

A	Hyposplenism
B	Hereditary elliptocytosis (HE)
C	Hereditary spherocytosis (HS)
D	Heinz body haemolytic anaemia
E	Sickle cell anaemia

6339

Submit

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C Hereditary spherocytosis (HS)

The blood film shows spherocytes which have a lack of central pallor seen in normal red blood cells, and a reduced diameter: this is the picture of hereditary spherocytosis. This disorder of the red cell membrane leads to spherical red blood cells with osmotic fragility, resulting in chronic haemolysis. HS is a heterogeneous group of disorders with regard to clinical severity, protein defects and mode of inheritance. It is relatively common in Caucasian populations; most affected individuals having mild or only moderate haemolysis. It may present in childhood with jaundice, but milder cases may go undiagnosed until early adulthood. There is usually a family history and a typical clinical and laboratory picture, so that the diagnosis is often easily made without additional laboratory tests. Moderately and severely affected individuals are likely to benefit from splenectomy, which should be performed after the age of 6 years and with appropriate

likely to benefit from splenectomy, which should be performed after the age of 6 years and with appropriate counselling about the infection risk. It is particularly important to rule out stomatocytosis, where splenectomy is contraindicated because of the thrombotic risk.

A Hyposplenism

Features of hyposplenism include Howell-Jolly bodies, Pappenheimer bodies, target cells and irregular contracted red blood cells, rather than the spherocytes seen here.

B Hereditary elliptocytosis (HE)

HS is commoner than HE, and loss of central pallor when erythrocytes are examined is less prominent in HE than in HS.

D Heinz body haemolytic anaemia

the spherocytes seen here.

B Hereditary elliptocytosis (HE)

HS is commoner than HE, and loss of central pallor when erythrocytes are examined is less prominent in HE than in HS.

D Heinz body haemolytic anaemia

Heinz bodies are inclusion bodies seen in red blood cells and they represent denatured DNA.

E Sickle cell anaemia

Blood films in sickle cell anaemia show features of hyposplenism and may show sickled red blood cells.

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A 79-year-old man is flagged by the Haematology Service because his routine international normalised ratio (INR) monitoring has revealed an INR of 10.8. He normally takes 7 mg warfarin per day for atrial fibrillation.

You call him at home and he is well, apart from some mild indigestion and bleeding around his gums.

On examination, his blood pressure (BP) is 132/82 mmHg and he looks well.

Investigations:

Haemoglobin (Hb)	12.1 g/dl
White cell count (WCC)	4.5 × 10^9/l
Platelets (PLT)	201 × 10^9/l
Sodium (Na^+)	141 mmol/l
Potassium (K^+)	4.9 mmol/l
Creatinine (Cr)	110 µmol/l
Faecal occult blood	Negative

Which of the following is the most

Platelets (PLT)	201×10^9/l
Sodium (Na^+)	141 mmol/l
Potassium (K^+)	4.9 mmol/l
Creatinine (Cr)	110 µmol/l
Faecal occult blood	Negative

Which of the following is the most appropriate course of management?

A	Low-dose vitamin K and stop warfarin
B	Fresh frozen plasma (FFP)
C	Prothrombin complex
D	Stop warfarin
E	Reduce warfarin dose to 3 mg

21175

warfarin per day for atrial fibrillation.

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On examination, his blood pressure (BP) is 132/82 mmHg and he looks well.

Investigations:

Haemoglobin (Hb)	12.1 g/dl
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Sodium (Na^+)	141 mmol/l
Potassium (K^+)	4.9 mmol/l
Creatinine (Cr)	110 µmol/l
Faecal occult blood	Negative

Which of the following is the most appropriate course of management?

Your answer was correct

A	Low-dose vitamin K and stop warfarin

The correct answer is Low-dose vitamin K and stop warfarin (Option A).

For many years, it was thought that low-dose vitamin K would interfere with rewarfarinisation; however, in practice, this is not a major problem. This has resulted in a change in guidelines over recent years, with most now recommending low-dose vitamin K with warfarin cessation when the INR is > 8 and there is minor bleeding.

B	Fresh frozen plasma (FFP)

Fresh frozen plasma (FFP) (Option B) is incorrect.

For the immediate reversal of INR in anticoagulated patients who are actively bleeding, prothrombin complex concentrates are preferred over FFP. FFP should only be used if more effective alternative treatments, such as prothrombin complex, are not

12:40

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2000 ml or > 30% of blood volume, it is recommended that prothrombin complex should be given in conjunction with vitamin K.

D Stop warfarin

Stop warfarin (Option D) is incorrect.

Simply stopping warfarin is not recommended in situations where the INR has such high values. Omitting warfarin is recommended for INR values of between 4.5 and 10 in patients with a low risk of bleeding or in patients where bleeding is present, but minor, and the INR value is < 4.5.

E Reduce warfarin dose to 3 mg

Reduce warfarin dose to 3 mg (Option E) is incorrect.

Reducing the dose of warfarin is recommended in cases where the INR is < 4.5 and patients have no active signs of bleeding.

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Question 1 of 60

INR	1.2
APTT	27 s
Urea	10 mmol/l
Creatinine	130 µmol/l
Liver function tests	Normal

Which of the following is the most likely explanation for his presentation and blood results?

A	Disseminated intravascular coagulation
B	Post-transfusion purpura
C	Heparin-induced thrombocytopaenia
D	Thrombotic thombocytopenic purpura
E	Immune thrombocytopaenic purpura

Question 1 of 60

A 60-year-old man received unfractionated heparin perioperatively following a routine knee replacement. He was not known to have any cardiovascular risk factors. His blood pressure preoperatively was 130/80 mmHg.

He was slow to mobilise, and 4 days post-operatively developed a large wound haematoma and the heparin was stopped. The patient required a transfusion of two units of blood and decompression of the wound. He was not known to have a history of bleeding problems and the operation otherwise was uncomplicated. All preoperative blood tests were normal.

A few days later, the patient is readmitted with right-sided chest pain and shortness of breath.

Chest X-ray was unremarkable.

Investigations:

Hb	11 g/dl
WCC	12 × 10^9/l
PLT	7 × 10^9/l

Question 1 of 60

C Heparin-induced thrombocytopaenia

Heparin-induced thrombocytopenia (HIT) is a severe, immune-mediated drug reaction that can occur in any patient exposed to heparin. This includes patients receiving unfractionated heparin (at both full therapeutic doses and low prophylactic doses, including the minute amounts in heparin flushes and on heparin-coated catheters) and those receiving low-molecular weight heparin (LMWH). Antibodies usually develop after a patient has been on heparin for five or more days, but may develop sooner if there has been previous heparin exposure. Despite thrombocytopenia, bleeding is rare. HIT is strongly associated with thrombosis. Thrombo-embolic complications can be venous, arterial or both; these include deep venous thrombosis, pulmonary embolism, myocardial infarction, thrombotic stroke and occlusion of limb arteries. When HIT is suspected clinically

stroke and occlusion of limb arteries.

When HIT is suspected clinically, heparin should be stopped and an alternative anticoagulant commenced, such as danaparoid, lepirudin or argatroban, which do not cross-react with HIT antibodies.

Oral anticoagulation with warfarin should not be initiated for longer-term protection from further events until substantial platelet count recovery has occurred. HIT patients who are switched to warfarin alone after the discontinuation of heparin may paradoxically have worsening thrombosis and develop venous limb gangrene and skin necrosis.

The diagnosis of HIT remains a clinical one, supported by confirmatory laboratory testing. The criteria include:

- thrombocytopenia (i.e. a drop in the platelet count to below 100 × 10^9/l or a drop of >50% from the patient's baseline platelet count)
- the exclusion of other causes of thrombocytopenia
- the resolution of

- the resolution of thrombocytopenia after cessation of heparin.

Regarding the laboratory tests, HIT antibodies can be demonstrated in vitro by functional tests and immunoassays. Functional tests, which measure platelet activity in the presence of the patient's serum and heparin, including heparin-induced platelet aggregation (HIPA) and the serotonin release assay (SRA), are more specific than the immunoassays and are therefore preferred in the diagnosis of HIT.

A	Disseminated intravascular coagulation

Disseminated intravascular coagulation (DIC) is a complex systemic thrombo-haemorrhagic disorder involving the generation of intravascular fibrin and the consumption of procoagulants and platelets. It is seen in association with a number of well-defined clinical

number of well-defined clinical situations, including sepsis, major trauma and abruptio placenta. It is associated with prolonged clotting times, low fibrinogen, raised fibrin degradation products and thrombocytopenia.

B	Post-transfusion purpura

Post-transfusion purpura (PTP) is an adverse reaction to a blood transfusion or platelet transfusion that occurs when the body produces allo-antibodies to the introduced platelets' antigens. These allo-antibodies destroy the patient's platelets, leading to thrombocytopenia. PTP usually presents 5–12 days after transfusion, and is therefore not relevant in this case.

D	Thrombotic thombocytopenic purpura

Thrombotic thrombocytopenic purpura (TTP) is a life-threatening

A 67-year-old woman is admitted with a large haematoma of the right arm after minimal trauma. She has noticed over the past few weeks increased bruising of the skin. The patient has recently completed a course of penicillin for a chest infection. She has a past history of psoriasis and hypertension.

Examination reveals multiple bruises and a large painful haematoma in the right upper arm. The venepuncture site displays prolonged bleeding.

Investigations:

Hb	10.2 g/dl
WCC	9.8 x $10^9/l$
PLT	325 x $10^9/l$
INR	1.0
APPT	53 s (30–40); does not correct with the addition of normal plasma

What is the most likely diagnosis?

5:05

Question 2 of 60

WCC	9.8 x 10^9/l
PLT	325 x 10^9/l
INR	1.0
APPT	53 s (30–40); does not correct with the addition of normal plasma

What is the most likely diagnosis?

A	Von Willebrand’s disease
B	Haemophilia A
C	Haemophilia B
D	Anti-phospholipid antibody syndrome
E	Acquired factor VIII deficiency

7076

Submit

E	Acquired factor VIII deficiency

Acquired factor VIII deficiency results from the development of antibodies against factor VIII, which prevent its action. This can occur in the elderly and is associated with malignancy, psoriasis, pemphigus and drugs (cephalosporins, penicillins). Patients develop bleeding tendencies and the activated partial thromboplastin time (APTT) is prolonged (intrinsic pathway). The APTT doesn’t correct/will only correct slightly with the addition of normal plasma. The Bethesda titre can quantify the inhibitor. There is a 20% mortality rate from acquired factor VIII deficiency.

A	Von Willebrand’s disease

Although Von Willebrand’s disease is associated with prolongation of APTT in 50% of patients due to low levels of factor VIII, it corrects on mixing with normal plasma.

B	Haemophilia A

Although haemophilia A does lead to bleeding and is associated with prolongation of APTT, presentation for the first time at this stage would be very unusual, and correction with normal plasma would be expected.

C	Haemophilia B

Haemophilia B is associated with bleeding, although correction of clotting disorder on mixing with normal plasma would be expected.

D	Anti-phospholipid antibody syndrome

APAS is associated with a prolonged APTT, although it results in a propensity towards thrombosis rather than increased risk of bleeding.

7076

Question 3 of 60

A 29-year-old patient who has undergone a bone marrow transplant for previous acute myeloid leukaemia presents for review complaining of increased bruising.

On examination, she has a number of areas of bruising and looks pale; her BP is 142/84 mmHg.

Investigations:

Hb	10.9 g/dl
WCC	3.9×10^9/l
PLT	6.0×10^9/l
Na^+	141 mmol/l
K^+	4.9 mmol/l
Creatinine	121 μmol/l

Which of the following is the most appropriate form of platelets to use for transfusion?

A	Washed

K⁺	4.9 mmol/l
Creatinine	121 µmol/l

Which of the following is the most appropriate form of platelets to use for transfusion?

A	Washed
B	HLA-matched
C	Family donated
D	Gamma-irradiated
E	Leukocyte-depleted

21174

Patients who have undergone bone marrow transplantation are at increased risk of transfusion-associated graft-versus-host disease (GVHD) because of lymphocytes within the donor material. Gamma-irradiated blood products are generally recommended for patients undergoing HLA-matched transfusions and those with an inherited immune system disorder, acquired immune disorder such as Hodgkin's disease or post bone-marrow transplantation. The irradiation minimises the chances of surviving leukocytes being found within the donated platelets.

A	Washed

Platelet washing is designed to remove about 99% of plasma. It does, however, result in decreased quality of platelet function, is labour- and time-intensive and can result in delays to transfusion.

B	HLA-matched

A 40-year-old woman presents with enlarging lumps in her neck. She first noticed them 6 weeks ago after a viral infection, but they have persisted and she feels they are enlarging.

She has lost 2 kg in weight and has had fevers that necessitate changing of the bedding two or three times per week. She has no previous medical history of note and is on no medication. She works full-time as a secretary, lives alone and keeps several cats (which she says regularly scratch her).

On examination, she has two 3 cm supraclavicular lymph nodes but no other obviously palpable disease. Chest X-ray shows mediastinal widening.

Investigations:

Hb	11.3 g/dl
WCC	3.5×10^9/l
PLT	170×10^9/l
Eosinophils	0.7×10^9/l (0.04–0.4)

WCC	3.5 × 10⁹/l
PLT	170 × 10⁹/l
Eosinophils	0.7 × 10⁹/l (0.04–0.4)
Lymphocytes	1.5 × 10⁹/l (1.5–4.0)

What investigation is most likely to be diagnostic?

A Bone marrow aspirate and trephine

B Fine needle aspiration of supraclavicular lymph nodes with immunocytochemistry

C Mediastinoscopy with biopsy

D Removal of entire supraclavicular lymph node for histological examination

E Serology for antibodies to *Bartonella henselae*

D Removal of entire supraclavicular lymph node for histological examination

This woman is likely to have lymphoma; although cat scratch fever is possible it rarely involves the mediastinum and the ‘B’ symptoms are dramatic. Removal of an entire lymph node is preferable to tru-cut biopsy: lymphoma diagnosis is fraught with technical difficulties and when subject to central review up to 30% of lymphomas are mis-classified, so every effort should be made to get the best biopsy specimen possible.

E Serology for antibodies to *Bartonella henselae*

A positive IgM test strongly suggests acute disease (or very recent infection) of cat scratch fever, but the production of IgM is usually brief. Thus, the serological diagnosis of acute infection can be elusive. However, a negative serologic test should not rule out CSD

can be elusive. However, a negative serologic test should not rule out CSD if there is a high clinical suspicion for disease. Prevalence of positive *Bartonella* serology in the general population is 4–6%, which creates false-positive test results. In this case the diagnosis is lymphoma, and therefore serology for antibodies to *B. henselae* is incorrect.

A	Bone marrow aspirate and trephine

Bone marrow examination is part of the staging of lymphoma, but would only be used for diagnostic purposes if there were no tissue accessible to biopsy.

B	Fine needle aspiration of supraclavicular lymph nodes with immunocytochemistry

Fine needle aspiration of lymph nodes is appropriate where nasopharyngeal carcinoma is suspected, but has a poor specificity/sensitivity in lymphoma.

A 40-year-old female patient on the Haematology Ward has become increasingly unwell over the past few days. She is 2 weeks' post-allogenic haemopoietic stem cell transplant (HSCT) for acute myeloid leukaemia.

On examination, she is jaundiced with ascites, hepatomegaly and right upper quadrant tenderness. Further examination reveals bi-basal inspiratory crepitations and peripheral oedema.

Initial investigations:

Hb	8.9 g/dl (120–155)
WCC	2.8 × 10^9/l (4.0–11.0)
Neutrophil count	1.8 × 10^9/l (2.0–7.5)
PLT	60 × 10^9/l (150–450)
Bilirubin	119 µmol/l (3–17)
ALT	39 IU/l (<40)
ALP	290 IU/l (40–130)
GGT	260 IU/l (10–50)

Albumin	28 g/l (35–50)
CRP	9 mg/l (<5)
Portable chest X-ray	Upper lobe diversion with blunted right costophrenic angle
Pre and post-transplant viral screens	-

What is the most likely diagnosis?

A	Veno-occlusive disease of the liver
B	Hepatitis B infection
C	Transfusion-associated cardiac overload (TACO)
D	Cyclosporin toxicity
E	Cholangitis

Question 5 of 60

A man aged 62 years is referred to the Haematology Clinic for review. He received a routine blood screen from his general practitioner (GP) that revealed a raised erythrocyte sedimentation rate (ESR) (85 mm/h) and a raised immunoglobulin G (IgG) paraprotein band (1.9 g/l). No urinary light chain excretion was detected.

Three years later, he remains well; however, he still has an increased ESR and IgG paraprotein band, though there is still no urinary light chain excretion.

Which of the following diagnoses fit best with this clinical picture?

A Waldenstrom's macroglobulinaemia

B Monoclonal gammopathy of unknown significance (MGUS)

C Myeloma

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Which of the following diagnoses fit best with this clinical picture?

A	Waldenstrom's macroglobulinaemia
B	Monoclonal gammopathy of unknown significance (MGUS)
C	Myeloma
D	B-cell lymphoma
E	Chronic myeloid leukaemia

33307

B	Monoclonal gammopathy of unknown significance (MGUS)

MGUS occurs in older people and is characterised by the presence of a paraprotein band (immunoglobulin G [IgG] <20 g/l). Patients may be asymptomatic and the condition discovered by chance. Blood count is usually normal, and there is no renal dysfunction. No specific treatment is required. Around 1% of patients with MGUS may progress to myeloma annually. In many patients with disease progression, immunoglobulin (Ig) gene rearrangement can be detected in B lymphocytes before the appearance of myeloma. This suggests that MGUS is a clonal, pre-malignant condition.

A	Waldenstrom’s macroglobulinaemia

This is one of the malignant monoclonal gammopathies and is a chronic, indolent, lymphoproliferative disorder. It is characterised by the

chronic, indolent, lymphoproliferative disorder. It is characterised by the presence of a high level of a macroglobulin (immunoglobulin M [IgM]), elevated serum viscosity and the presence of a lymphoplasmacytic infiltrate in the bone marrow.

C	Myeloma

There is no light chain excretion in the urine that would confirm the diagnosis of myeloma, and no organ involvement (e.g. bone, liver, spleen).

D	B-cell lymphoma

Non-Hodgkin's lymphoma is a collective term for a heterogeneous group of lymphoproliferative malignancies with differing patterns of behaviour and responses to treatment. Most NHLs (80–85%) are of B-cell origin. There is no distinct paraprotein in the serum electrophoresis, but there may be a diffuse increase in the IgG region.

Question 6 of 60

A 40-year-old woman presents with a 24 h history of unilateral swelling of the left leg. She has recently flown back to this country from Australia. She is previously fit and well, does not smoke and is on no medication. She has no family history of note.

Other than the swollen leg, examination is unremarkable. Ultrasound of the deep veins of the leg confirms an above-knee deep vein thrombosis, and she is commenced on enoxaparin 1.5 mg/kg daily subcutaneously and started on 10 mg of warfarin. On the second day after starting warfarin she has developed black lesions over her buttocks. Platelet count remains stable at 205 × 10^9/l.

What is the most likely cause of the lesions over her buttocks?

A Heparin-induced thrombocytopenia type 2

B Protein C deficiency

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What is the most likely cause of the lesions over her buttocks?

A	Heparin-induced thrombocytopenia type 2
B	Protein C deficiency
C	Prothrombin gene 20210 mutation
D	Antithrombin III deficiency
E	Anti-phospholipid antibody syndrome

6306

Question 6 of 60

Other than the swollen leg, examination is unremarkable. Ultrasound of the deep veins of the leg confirms an above-knee deep vein thrombosis, and she is commenced on enoxaparin 1.5 mg/kg daily subcutaneously and started on 10 mg of warfarin. On the second day after starting warfarin she has developed black lesions over her buttocks. Platelet count remains stable at 205 × 10^9/l.

What is the most likely cause of the lesions over her buttocks?

Your answer was incorrect

A	Heparin-induced thrombocytopenia type 2
B	Protein C deficiency
C	Prothrombin gene 20210 mutation

B Protein C deficiency

This lady has developed warfarin-induced skin necrosis (WISN); this occurs when warfarin is started and there is a defect in the protein C anticoagulant pathway. Protein C is vitamin K dependent and falls rapidly following the commencement of warfarin, leading to an initial paradoxical prothrombotic state: this explains why heparin is started concurrently with warfarin, to cover this initial period. The condition has been reported in association with most forms of thrombophilia, but defects in the protein C pathway (classically protein C deficiency, but also including protein S and activated protein C resistance) are the most common pre-existing conditions. Microthrombi form in the blood vessels of the skin, particularly in adipose areas such as buttocks and breast. The condition is severe, and plastic surgery is often required. Treatment is supportive, with vitamin K and possibly fresh frozen plasma to replace protein C levels.

Prostacyclin and protein C infusion have been trialled. Warfarin can be reintroduced at a lower loading dose, but recurrence may occur.

C Prothrombin gene 20210 mutation

The prothrombin gene 20210 mutation is a cause of thrombophilia, rather than a cause of protein C deficiency in association with warfarin initiation.

A Heparin-induced thrombocytopenia type 2

HIT is associated with the development of necrotic skin ulcers, although the maintenance of a stable platelet count counts against this as the underlying diagnosis.

D Antithrombin III deficiency

Antithrombin III deficiency is associated with recurrent thrombosis, and is seen as an autosomal dominant

diagnosis.

D	Antithrombin III deficiency

Antithrombin III deficiency is associated with recurrent thrombosis, and is seen as an autosomal dominant congenital disorder and in patients with severe proteinuria. It is not associated with commencement of warfarin.

E	Anti-phospholipid antibody syndrome

This occurs either in isolation or against a background of SLE and is associated with recurrent venous thrombosis and other features such as livedo reticularis.

6306

Question 7 of 60

A 33-year-old ward sister who is currently on an oral contraceptive pill (OCP) is requesting sterilisation, as she is concerned about the risks of venous thrombosis involved with the OCP.

Her maternal aunt at the age of 65 years developed pulmonary embolism following her knee surgery, for which she was anticoagulated. Her aunt went on to have subsequent screening of pro-coagulant tendencies, and heterozygous factor V Leiden was identified. The patient's mother has suffered no problems, having had three normal pregnancies and varicose veins only.

What advice would you give the patient?

A Reassure and inform the patient that risk is minimal in continuing OCP

B Stop OCP immediately and seek gynaecological operation for sterilisation

heterozygous factor V Leiden was identified. The patient’s mother has suffered no problems, having had three normal pregnancies and varicose veins only.

What advice would you give the patient?

A Reassure and inform the patient that risk is minimal in continuing OCP

B Stop OCP immediately and seek gynaecological operation for sterilisation

C Use other methods of contraception

D Finish current pill pack and then continue with progesterone-only pill

E Check for factor V Leiden and if positive stop OCP

E Check for factor V Leiden and if positive stop OCP

About 5% of the UK population carry a factor V Leiden mutation. The mutation slows the normal breakdown of factor V, leading increased circulating thrombin levels. Heterozygotes for the mutation have a slightly increased risk of developing venous thromboembolism, but most will never have any clinically relevant episode. Heterozygote carriers have 4–8-fold increased risk of venous thrombo-embolism (VTE), and homozygous carriers have an 80-fold increased risk. Women who take the OCP, however, have a significantly raised risk of venous thrombosis and currently the use of any type OCP in women with confirmed factor V Leiden is not recommended.

C Use other methods of contraception

A switch of contraception may not be

Question 7 of 60

A switch of contraception may not be required in the event that screening for factor V Leiden is negative. Hence a switch of contraception without screening isn't needed.

A	Reassure and inform the patient that risk is minimal in continuing OCP

From the point of view of relatives known to be affected by VTE, screening of patients for mutation is recommended. If a mutation is found, then non-hormonal contraception should be recommended unless a woman has completed her family and expresses a preference for sterilisation.

B	Stop OCP immediately and seek gynaecological operation for sterilisation

It may be appropriate to continue the OCP in the event that screening for thrombophilia is negative.

Question 7 of 60

recommended. If a mutation is found, then non-hormonal contraception should be recommended unless a woman has completed her family and expresses a preference for sterilisation.

B	Stop OCP immediately and seek gynaecological operation for sterilisation

It may be appropriate to continue the OCP in the event that screening for thrombophilia is negative.

D	Finish current pill pack and then continue with progesterone-only pill

Switching to the POP would be an option, although it is less effective than the combined oral contraceptive pill with respect to contraception. Hence a switch isn't advised unless the patient has prothrombotic tendencies.

9843

Rate this question: ⊖ ☆☆☆☆☆

PLT	450 × 10^9/l
CXR	New shadowing at right base

He is diagnosed with acute chest syndrome, possibly related to mycoplasma infection.

What intervention has been shown to reduce the incidence of acute chest syndrome?

A Low-dose enoxaparin

B Prophylactic clarithromycin

C Hydroxyurea

D Folate supplements

E Low-dose aspirin

33317

Question 8 of 60

C Hydroxyurea

The appearance of a new pulmonary infiltrate on the chest radiograph of a patient with sickle cell disease is termed ‘acute chest syndrome’. The syndrome can develop because of infection, infarction or a combination of the two. Infectious causes include Gram-positive or -negative bacteria, atypical bacteria and viruses. The usual organisms include *Pneumococcus*, *Mycoplasma* and *Chlamydia*. Acute chest syndrome is usually accompanied or preceded by pain in the chest or extremities, fever, respiratory distress and/or low oxygen saturation. The white blood cell count is generally high. Although the chest radiograph may be normal initially, subsequent radiographs will reveal an infiltrate, which may extend rapidly, involving one or more lobes as well as the pleura.

One randomised control trial in adults found that hydroxyurea reduced acute chest syndrome and the need for blood transfusion in people with sickle

blood transfusion in people with sickle cell disease over a mean of 21 months. It found no significant difference in stroke, hepatic sequestration and mortality related to sickle cell disease between hydroxyurea and placebo, but the sample size is likely to have been too small to draw any conclusions in this respect.

B Prophylactic clarithromycin

Empirical antibiotics should be initiated and given intravenously, after obtaining samples for appropriate cultures. If women with sickle cell disease have not undergone a preconceptual review, they should be advised to take daily folic acid and prophylactic antibiotics (if not contraindicated).

A Low-dose enoxaparin

This is not indicated for the management of acute chest syndrome. There is not enough evidence in the literature supporting the use of low-

literature supporting the use of low-molecular weight heparin in the management of sickle cell crisis. A few studies demonstrated that it may reduce the painful symptoms, but the data were not sufficient for it to be used routinely in clinical practice. Women with sickle cell disease should be advised to receive prophylactic low-molecular weight heparin during antenatal hospital admissions.

D	Folate supplements

Long-term folate supplementation is recommended for patients with sickle cell anaemia and also during pregnancy, but not for the acute management of acute chest syndrome.

E	Low-dose aspirin

This is not recommended as part of the management of the acute chest syndrome. Women with sickle cell disease should be considered for low-dose aspirin 75 mg once daily from 12

Question 9 of 60

A 38-year-old nurse is admitted to the Emergency department of her local hospital having begun feeling very unwell whilst eating a fruit salad. She takes a calcium channel blocker for hypertension but is on no other medications of note. She has wheeze and stridor, and generalised erythema. Her BP is 95/60 mmHg and her pulse is 98/min and regular. She is treated with adrenaline and hydrocortisone.

Which of the following blood tests taken at the time of an attack may be useful in confirming anaphylaxis?

A Eosinophil count

B IgE

C Mast cell tryptase

D Histamine

E Cortisol

C Mast cell tryptase

Tryptase is a trypsin-like proteinase that is found mostly in mast cells and basophils, with the former containing almost 300 times more tryptase than the latter. As such, tryptase is specific to mast cell granules and can provide information about mast cell number, distribution and activation depending on the clinical context. Tryptase exerts sequential actions similar to histamine, namely as a vasoactive, pro-inflammatory and chemotactic substance. Mast cell tryptase is measured within 1–2 h of an episode of anaphylaxis and is the preferred measure of mast cell degranulation. Acute management of anaphylaxis includes SC or IM adrenalin, coupled with IV hydrocortisone and antihistamine. In this case, the patient’s occupation as a nurse raises the possibility of latex fruit syndrome.

A Eosinophil count

Question 9 of 60

Mild eosinophilia can be seen in allergic diseases, including allergic rhinitis, atopic asthma and atopic dermatitis. It is not a specific marker capable of confirming the diagnosis of anaphylaxis. Markedly raised eosinophil count (>1500 mm^3) is characteristic of the hypereosinophilic syndromes, which are a heterogeneous group of disorders presenting with persistent eosinophilia and/or evidence of end organ damage after exclusion of known causes of eosinophilia, including parasitic infections and drug reactions.

B	IgE

Elevated IgE levels are seen in patients with atopic diseases, with the highest levels generally being seen in atopic dermatitis, followed by atopic asthma, perennial allergic rhinitis and seasonal allergic rhinitis. Elevated IgE levels are also seen in other disorders, including parasitic infections (e.g. strongyloidiasis, ascariasis, schistosomiasis), non-parasitic

infections (e.g. EBV, CMV, HIV, *Mycobacterium tuberculosis*) and haematological malignancies (e.g. Hodgkin's lymphoma, IgE myeloma. For seasonal allergens, peak IgE levels occur 4–6 weeks after the peak of pollen season; therefore raised IgE levels are neither a direct nor a specific marker for anaphylaxis.

D	Histamine

Histamine is an endogenous biogenic amine present in high concentrations in the lungs, skin and gastrointestinal tract. Histamine is synthesised and stored at high concentrations within granules in basophils and mast cells, where it is associated with heparin. In addition, non-mast cell histamine occurs at high concentrations in enterochromaffin-like cells in the stomach, lymph nodes and thymus, with modest levels in the liver, lung and in varicosities of the histaminergic neurons in the brain. Histamine acts as a neurotransmitter in the nervous system and as a local mediator in the

neurons in the brain. Histamine acts as a neurotransmitter in the nervous system and as a local mediator in the gut, skin and immune system. Its functions include neurotransmission, inflammation, smooth muscle contraction, dilatation of capillaries, chemotaxis, cytokine production and gastric acid secretion. There is no evidence that measurement of histamine levels will be useful in confirming anaphylaxis. Whilst histamine is also elevated, the rise in histamine seen in association with anaphylaxis is much more transient.

E	Cortisol

Any stress response leads to an elevation of cortisol, which therefore is not a specific marker for confirming anaphylaxis.

36023

A 40-year-old woman presents with indigestion of seven weeks’ duration. She has no ongoing medical problems, and is otherwise asymptomatic. She is on no medication.

Examination is unremarkable. She undergoes gastro-oesophageal endoscopy, which reveals gastritis. Stomach biopsies confirm the presence of a mucosa-associated lymphoid tissue lymphoma (maltoma/marginal zone lymphoma) of low-grade type; *Helicobacter pylori* is demonstrated. Computed tomography (CT) of chest, abdomen and pelvis reveals no additional disease, and a bone marrow trephine is unremarkable; the stomach wall is not clearly thickened.

What treatment would you recommend?

A	Cyclophosphamide, vincristine, doxorubicin and prednisolone (CHOP)
B	Observation alone

disease, and a bone marrow trephine is unremarkable; the stomach wall is not clearly thickened.

What treatment would you recommend?

- A Cyclophosphamide, vincristine, doxorubicin and prednisolone (CHOP)
- B Observation alone
- C *H. pylori* eradication therapy
- D Partial gastrectomy
- E High-dose dexamethasone

Question 10 of 60

C H. *pylori* eradication therapy

Maltomas, also known as marginal zone lymphomas, are low-grade lymphomas, most often diagnosed in the stomach. They are peculiar in that they are often associated with chronic inflammation of one of the following types:

- In the stomach secondary to chronic *H. pylori* gastritis
- In the eyes secondary to Sjogren syndrome
- In the thyroid secondary to Hashimoto’s thyroiditis
- In the intestine secondary to Crohn’s or coeliac disease.

Treatment against *H. pylori* is safe and will cause regression in 90% of low-grade gastric maltomas; response is less likely if cytogenetic abnormalities have been acquired (t11:18 being the most common), or if the muscularis mucosa has been invaded. This patient has early-stage disease, so triple

has early-stage disease, so triple therapy coupled with close oncological and gastroenterological follow-up is appropriate.

A Cyclophosphamide, vincristine, doxorubicin and prednisolone (CHOP)

R-CHOP (including rituximab) is a treatment option for more advanced gastric lymphoma.

B Observation alone

Observation alone risks significant lymphoma progression, meaning that *H. pylori* eradication would then in all likelihood be ineffective.

D Partial gastrectomy

Surgery is rarely employed in the treatment of gastric maltoma, because it is usually not curative and results in significant operative morbidity.

A 60-year-old woman is referred with symptoms of generalised malaise. She feels lethargic and breathless on moderate exertion. She has also noticed increased bleeding of her gums on brushing her teeth and has had several chest infections over the past month.

Past history is of diabetes, hypertension and gout.

Investigations:

Hb	8.6 g/dl
WCC	3.5 x 10^9/l
PLT	64 x 10^9/l
Bone marrow aspirate	Myeloid blast cells
Chromosome analysis	t(15:17) translocation

What is the most likely diagnosis?

A	Chronic myeloid leukaemia

Question 11 of 60

WCC	3.5 x 10^9/l
PLT	64 x 10^9/l
Bone marrow aspirate	Myeloid blast cells
Chromosome analysis	t(15:17) translocation

What is the most likely diagnosis?

A	Chronic myeloid leukaemia
B	Acute promyelocytic leukaemia
C	Myelomonocytic leukaemia
D	Erythroleukaemia
E	Megacaryoblastic leukaemia

7077

B | Acute promyelocytic leukaemia

Acute promyelocytic leukaemia is also known as FAB (French–American–British) classification type M3. It characteristically denotes a translocation of t(15:17) that involves a retinoic acid receptor gene. This leukaemia is associated with disseminated intravascular coagulation, and can be treated initially with all-trans retinoic acid. The leukaemic cells are generally hypergranular promyelocytes. Other important translocations include:

t(8:14) – Burkitt's lymphoma

t(9:22) – Philadelphia chromosome in chronic myeloid leukaemia.

A | Chronic myeloid leukaemia

CML is associated with hepatosplenomegaly and with an increase in granulocytes at all stages of development, including eosinophils and basophils

C	Myelomonocytic leukaemia

In chronic myelomonocytic leukaemia an increase in the peripheral blood monocyte count is expected, which has not been seen here.

D	Erythroleukaemia

Erythroleukaemia does present with pancytopenia as has been seen here, but isn't associated with the t(15:17) translocation, which is typical for acute promyelocytic leukaemia.

E	Megacaryoblastic leukaemia

This is a rare condition where the majority of blast cells are megakaryoblastic. It is seen more commonly in patients with Down syndrome, and is associated with t(1;22)(p13;q13) in approximately 1/3 of cases.

7077

Rate this question: ⊖ ☆☆☆☆☆

Question 12 of 60

A 60-year-old woman with rheumatoid arthritis presents with breathlessness and chest pain, developing over a week.

Examination shows a pale, jaundiced patient in some distress, pulse 110 beats per minute (bpm) and third heart sound audible with jugular venous pressure raised. Widespread crackles are audible throughout the chest. There is a 3 cm spleen palpable. An electrocardiogram shows widespread depression of ST segments.

Investigations:

Hb	4.9 g/dl
MCV	105 fl (80–96)
Coombs’ test	IgG+
Bilirubin	45 µmol/l (1–22)
LDH	1157 U/l (10–250)

How would you best interpret these tests?

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LDH	1157 U/l (10-250)

How would you best interpret these tests?

A	Raised MCV is probably due to reticulocytosis
B	Urine examination for haemosiderin is likely to be positive
C	Haemolysis cannot be confidently ruled out unless the result of a haptoglobin assay is available
D	Raised LDH is most likely to be cardiac in origin
E	If haemolysis is truly present then close to 100% of bilirubin will be unconjugated

33302

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A Raised MCV is probably due to reticulocytosis

This patient has haemolytic anaemia (the IgG antibodies cause warm autoimmune haemolytic anaemia, i.e. the antibody is active at body temperature). Transfusion can be life-saving until immunosuppression can take effect. The bone marrow responds by increasing red cell production; this is in evidence in the peripheral blood by an increase in reticulocytes – immature red blood cells, which have a larger MCV. All patients with active haemolysis are at risk of acquiring folate deficiency due to increased metabolic demands, and all should receive replacement therapy.

B Urine examination for haemosiderin is likely to be positive

The haemolysis occurs extravascularly (e.g. in the liver and spleen), so measures of intravascular haemolysis

urinary haemosiderin) will be negative.

C Haemolysis cannot be confidently ruled out unless the result of a haptoglobin assay is available

The haptoglobins are not a specific marker for haemolysis since these can be decreased or absent in other conditions as well (e.g. genetics, cirrhosis, infancy, pregnancy, burns).

D Raised LDH is most likely to be cardiac in origin

LDH is increased in haemolysis, although in this patient it would be prudent to exclude a cardiac cause. It is most likely to be due to haemolysis, with the ischaemic picture on ECG being related to anaemia.

E If haemolysis is truly present then close to 100% of bilirubin will be unconjugated

Question 12 of 60

although in this patient it would be prudent to exclude a cardiac cause. It is most likely to be due to haemolysis, with the ischaemic picture on ECG being related to anaemia.

E	If haemolysis is truly present then close to 100% of bilirubin will be unconjugated

In haemolytic anaemia there is an excess of unconjugated bilirubin in the blood; because the unconjugated bilirubin is not water soluble, one will not see an increase in bilirubin in the urine. Since there is no problem with the liver or bile systems, this excess unconjugated bilirubin will go through all of the normal processing mechanisms that occur (i.e. conjugation, excretion in bile, metabolism to urobilinogen, reabsorption) and will show up as an increase in urine urobilinogen.

33302

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A 45-year-old Cypriot man attends his GP for a new patient appointment. He feels well and works long hours running a painting and decorating business.

The only past history of note is mild hypertension, for which he has been recommended to lose weight and institute lifestyle improvements.

Investigations:

Hb	7.0 g/dl (MCV 68; target cells)
WCC	4.9 × 10^9/l
PLT	190 × 10^9/l
Na$^+$	140 mmol/l
K$^+$	5.0 mmol/l
Creatinine	130 μmol/l
HbF	Slightly elevated
HbA2	Normal
Faecal occult blood	+

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Creatinine	130 µmol/l
HbF	Slightly elevated
HbA2	Normal
Faecal occult blood	+

Which of the following is the most likely diagnosis?

A Lead poisoning

B Beta-thalassaemia minor

C Iron deficiency anaemia

D Co-existent beta-thalassaemia minor and iron deficiency anaemia

E Hereditary spherocytosis

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D Co-existent beta-thalassaemia minor and iron deficiency anaemia

We are given various clues to the diagnosis here: his nationality points us towards the possibility of thalassaemia minor, yet the anaemia seems unexpectedly severe and HbA2 levels are normal, which is out of keeping with the diagnosis. The faecal occult blood positivity, however, suggests the possibility of co-existent GI tract blood loss, and in cases of severe iron deficiency anaemia the HbA2 may be normal in thalassaemia minor. Hence he requires adequate investigation of his iron status, with iron studies and imaging of the GI tract to rule out occult GI blood loss.

B Beta-thalassaemia minor

Beta-thalassaemia minor may be associated with microcytosis, but wouldn’t fit with the positive faecal occult blood reported in this patient.

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wouldn’t fit with the positive faecal occult blood reported in this patient.

A	Lead poisoning

Lead poisoning is associated with microcytic anaemia, although it wouldn’t explain the positive faecal occult blood seen here.

C	Iron deficiency anaemia

Iron deficiency anaemia alone wouldn’t explain the significant reduction in MCV seen here with regard to the level of anaemia.

E	Hereditary spherocytosis

Hereditary spherocytosis is associated with haemolysis, not with microcytic anaemia and positive faecal occult bloods as in this patient.

21035

Rate this question: ⊖ ☆☆☆☆☆

Question 14 of 60

A 69-year-old retired headteacher with rapidly deteriorating back pain comes to see you in the clinic. The pain started 6 months ago following a fall down the stairs.

Lumbar spine X-ray then confirmed vertebral collapse of L2 and L4. She started calcium/vitamin D3 and a bisphosphonate. The pain has now spread to her thoracic spine. The pain does not vary with time of day or exercise. Although her appetite has decreased, her weight seems steady. She smoked in her youth. She has hypertension.

Current medication comprises regular opioid analgesia, a diuretic and a statin.

On examination, she is pale. Her cardiovascular, chest and abdominal investigations are normal. She is non-specifically tender over her thoracic and lumbar spine. Although her neurological examination is hindered by pain, nothing of note was found. Chest X-ray reveals a slightly enlarged cardiac shadow; T-spine, collapse of

Question 14 of 60

Chest X-ray reveals a slightly enlarged cardiac shadow; T-spine, collapse of T5; L-spine, collapse of L2, L4.

Investigations:

Hb	8.7 g/dl
WCC	3.4 × 10^9/l
PLT	124 × 10^9/l
Na^+	142 mmol/l
K^+	4.9 mmol/l
Creatinine	141 μmol/l
Urea	10.1 mmol/l
Ca^+	2.34 mmol/l
Albumin	36 g/l
Bilirubin	12 mmol/l
ALT	36 U/l
ALP	12 mmol/l
TP	84 g/l
PO_4	1.01 mmol/l

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ALP	12 mmol/l
TP	84 g/l
PO_4	1.01 mmol/l
ESR	42 mm/h
CRP	6 mg/l

A blood film shows a normocytic anaemia and some rouleaux formation. Urinalysis reveals 2+ of protein.

What is the most likely diagnosis?

A	Osteoporosis
B	Renal cell carcinoma
C	Multiple myeloma
D	Osteoporosis and over-diuresis
E	Squamous cell lung carcinoma

C Multiple myeloma

The rapidly increasing severity of back pain that does not vary with time or movement is significant. Although her calcium is not elevated, her globulins are (by virtue of the fact her total protein is raised and albumin is relatively normal), as is her ESR. She also has renal impairment and multiple areas of vertebral collapse.

Multiple myeloma is a disease in which there is accumulation of malignant plasma cells, generally derived from one clone in the bone marrow. It is characterised by the production of a monoclonal immunoglobulin that can be detected in the serum or urine. It is often associated with bone pain, kidney disease and anaemia.

Diagnostic tests include bone marrow examination, the presence of more than 10% plasma cells being required for diagnosis. A skeletal survey is required for lytic lesions and serum/urine electrophoresis is needed to identify the presence of paraprotein.

to identify the presence of paraprotein. Urinalysis can be performed to identify Bence Jones protein.

Treatment is based around melphalan chemotherapy. In patients under 65 years of age, bortezomib is often used as an induction therapy for those patients going on to high-dose chemotherapy and autologous stem cell transplantation, which often leads to a prolonged remission compared to conventional chemotherapy.

A Osteoporosis

Patients often present with back pain and fractures (including compression fractures) worsening slowly over time. The key points to note are the raised protein levels, renal impairment, raised ESR and proteinuria, which are not in keeping with a diagnosis of osteoporosis, meaning that this is incorrect.

B Renal cell carcinoma

Renal cell carcinomas can metastasise to the lymph nodes, bone, liver, lung and brain, so it would be one of the differentials for this patient. Renal cell cancer can present with bony involvement, anaemia and renal impairment, However, the protein level would usually be normal to low and the overall picture of this patient with raised ESR coupled with vertebral collapse and renal impairment, is more in keeping with a diagnosis of myeloma. Renal cell cancer patients often present with haematuria, unilateral abdominal pain, abdominal mass, fatigue, anorexia and weight loss.

D	Osteoporosis and over-diuresis

Osteoporosis tends to have a more insidious onset. This patient's picture is also not in keeping with a patient who has been over-diuresed. If that were the case, you would expect the patient to have a low sodium and potassium alongside a raised urea and creatinine.

5:46

Question 14 of 60

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D Osteoporosis and over-diuresis

Osteoporosis tends to have a more insidious onset. This patient’s picture is also not in keeping with a patient who has been over-diuresed. If that were the case, you would expect the patient to have a low sodium and potassium alongside a raised urea and creatinine.

insidious onset. This patient's picture is also not in keeping with a patient who has been over-diuresed. If that were the case, you would expect the patient to have a low sodium and potassium alongside a raised urea and creatinine. However, this patient has normal electrolyte levels.

E	Squamous cell lung carcinoma

This diagnosis is a possibility in this patient. The X-ray commented on an enlarged heart border, but an X-ray is unable to exclude a central mass. The cancer could have spread to the bone but you would usually expect a raised calcium, either secondary to bony involvement or due to a paraneoplastic phenomenon of hypercalcaemia of malignancy in squamous cell lung cancer. This patient's clinical picture does not quite fit with this and, as such, means it is not the most likely diagnosis for this patient.

2297

A 35-year-old woman is found to have a right-sided deep vein thrombosis (DVT) 3 days after an elective cholecystectomy. She had been started on prophylactic low-molecular weight heparin 2 days prior to the surgery.

Three years ago, she had also suffered a DVT in the same leg, affecting the calf, also following an operation. She had been warfarinised for several months following that incident.

Investigations:

Hb	12.8 g/dl
WCC	7.7 × 10⁹/l
PLT	178 × 10⁹/l
Na^+	140 mmol/l
K^+	4.5 mmol/l
Creatinine	110 µmol/l
PT	14 s
APTT	29 s

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Na⁺	140 mmol/l
K⁺	4.5 mmol/l
Creatinine	110 µmol/l
PT	14 s
APTT	29 s

How long should she be warfarinised for this time?

- A 6 weeks
- B 3 months
- C 6 months
- D 1 year
- E Lifelong

21539

C	6 months

In the absence of thrombophilia, the recommendation from guidelines for treatment of a second provoked DVT is 6 months of warfarin. The APTT is in the normal range, which reduces the likelihood of her suffering from anti-phospholipid antibody syndrome, although she may of course have an alternative inherited thrombophilic disorder such as the factor V Leiden mutation.

B	3 months

At least 3 months' anticoagulation is recommended for a first proximal lower limb DVT.

A	6 weeks

Six weeks' warfarinisation may be considered for the treatment of an isolated calf vein DVT.

Six weeks' warfarinisation may be considered for the treatment of an isolated calf vein DVT.

D	1 year

There is no value in giving longer than 6 months' anticoagulation unless the patient has life-long risk factors for further venous thromboembolism; in this case life-long anticoagulation rather than 1 year's treatment is recommended.

E	Lifelong

Recurrence of DVT whilst on warfarin would be an indication for life-long anticoagulation, as would diagnosis of a recognised cause of thrombophilia.

21539

An 18-year-old man presents to the Emergency Department with a haemarthrosis of his left knee after a relatively minor traumatic incident playing football in the park.

You understand from his sister that there have been a number of similar incidents over the past 10 years. The child is adopted, but you understand from previous notes that he may have a bleeding disorder which runs in the family.

Investigations:

Hb	12.1 g/dl
WCC	5.4 x 10^9/l
PLT	190 x 10^9/l
Factor VIII	Normal
PT	13.1 s
APTT	48 s
Bleeding time	Normal

Which of the following is the most likely diagnosis?

Factor VIII	Normal
PT	13.1 s
APTT	48 s
Bleeding time	Normal

Which of the following is the most likely diagnosis?

A	Von Willebrand's disease (VWD)
B	Haemophilia A
C	Acquired haemophilia
D	Haemophilia B
E	Glanzman thrombasthaenia

21034

D Haemophilia B

Haemophilia B, or inherited factor IX deficiency, is responsible for around 20% of cases of haemophilia. Patients usually present in childhood with easy bruising, prolonged bleeding after dental work or haemarthrosis after a relatively minor incident of trauma. Both haemophilia A and B are inherited as x-linked diseases, and as such only male individuals present with the bleeding disorder. Given that his factor VIII levels are normal, factor IX deficiency is the likely diagnosis. Cut-offs for classification of haemophilia range from less than 1% of normal levels of the clotting factor (severe), 1–5% (moderately severe) to 5–40% (mild).

A Von Willebrand's disease (VWD)

APTT is only mildly prolonged in 50% of patients with VWD, and it is therefore less likely to be the cause of

his symptoms versus haemophilia B.

B Haemophilia A

Haemophilia A is ruled out by the normal factor VIII levels seen here.

C Acquired haemophilia

Acquired haemophilia occurs later in life in patients with collagen vascular disease due to cross-reacting antibodies, and anti-clotting factor antibodies in patients treated for a number of years for haemophilia may lead to reduced effectiveness.

E Glanzman thrombasthaenia

Glanzmann's is a disorder of platelet function; it is an extremely rare coagulopathy in which the platelets contain defective or low levels of glycoprotein IIb/IIIa, a receptor for fibrinogen.

21034

Question 17 of 60

A 38-year-old woman with a history of systemic lupus erythematosus (SLE) presents with right-sided pleural chest pain and a dry cough, which she has had for 3 weeks.

On examination, she is apyrexial. Auscultation of the chest reveals normal breath sounds although shallow respiration is noted. Chest X-ray is normal.

On further questioning, she reveals that her SLE is usually well controlled and that all her SLE tests were normal when she was seen in clinic 3 months ago.

Investigations:

CRP	8 mg/l
Serum IgG	16.0 g/l (6.0–13.0)
Complement C_3	150 mg/dl (65–190)
Complement C_4	10 mg/dl (15–50)
$p_a(O_2)$	11.5 kPa
$p_a(CO_2)$	4.8 kPa

Complement C_3	150 mg/dl (65–190)
Complement C_4	10 mg/dl (15–50)
$p_a(O_2)$	11.5 kPa
$p_a(CO_2)$	4.8 kPa
oxygen saturation	98%

What is the most likely diagnosis?

A	Reactivation of SLE
B	*Pneumocystis jirovecii* pneumonia (PCP)
C	Pneumonia
D	Pulmonary embolus (PE)
E	Costochondritis

On examination, she is apyrexial. Auscultation of the chest reveals normal breath sounds although shallow respiration is noted. Chest X-ray is normal.

On further questioning, she reveals that her SLE is usually well controlled and that all her SLE tests were normal when she was seen in clinic 3 months ago.

Investigations:

CRP	8 mg/l
Serum IgG	16.0 g/l (6.0–13.0)
Complement C_3	150 mg/dl (65–190)
Complement C_4	10 mg/dl (15–50)
$p_a(O_2)$	11.5 kPa
$p_a(CO_2)$	4.8 kPa
oxygen saturation	98%

A Reactivation of SLE

Systemic lupus erythematosus is a relapsing and remitting non-organ-specific autoimmune disease characterised by vasculitis and the presence of antinuclear antibodies. Respiratory symptoms are common (in 65%), and these include non-infective pleurisy. Cases of pneumonia are also more common in the general population due to a relative immune paresis.

Early markers of SLE disease activity include falling C_4 levels, although congenital C_4 deficiency is itself a predisposing factor for SLE development, so these tests must be interpreted with caution. Other markers of disease activity include rising immunoglobulins, falling haemoglobin (Hb), white cell count (WCC), platelets and albumin.

B *Pneumocystis jirovecii* pneumonia (PCP)

PCP is an opportunistic infection associated with immunosuppression due to HIV, haematological disorders (especially leukaemia and post-bone marrow transplant) and oncology and renal transplantation. A decrease in oxygen saturation, as measured by pulse-oximetry during exercise, indicates PCP, especially when the patient doesn't appear acutely unwell and with minimal symptoms.

C	Pneumonia

Pneumonia is an unlikely diagnosis as there are no focal chest signs and CXR is normal. Pathogenic infection of the lungs presents with a productive cough and signs of hyperthermia, tachypnoea and tachycardia, with altered mental status.

D	Pulmonary embolus (PE)

PE may present with the similar symptoms, but ABG results may show reduced PaO_2 and $PaCO_2$. The classic

Question 17 of 60

D	Pulmonary embolus (PE)

PE may present with the similar symptoms, but ABG results may show reduced PaO_2 and $PaCO_2$. The classic findings are not useful in the diagnosis of PE. Many conditions also cause hypoxaemia, but hypocapnia usually is present with embolism; hypercapnia, on the other hand, is rare. A massive PE may show combined respiratory and metabolic acidosis due to circulatory collapse.

E	Costochondritis

This condition is diagnosed after other causes of pleuritic chest pain are ruled out. It presents with tenderness on palpation over the area where the chest pain is reported.

9845

An 18-year-old man presents to the Accident and Emergency Department with severe back pain that came on while he was ice-skating. He has recently recovered from a viral upper respiratory tract infection, but is otherwise fit and well. He developed back pain without any obvious trauma, and passed dark red urine: he has not passed urine since (four hours ago). He is on no medications and does not smoke or drink. There is no family history of note.

On examination, he is in severe discomfort, temperature 38.3 °C, pulse 120 beats per minute, blood pressure 145/83 mmHg, peripheries are well perfused and there is no cyanosis. He is icteric. Abdominal, respiratory and cardiovascular examinations are unremarkable.

Investigations:

Hb	8.3 g/dl
WCC	4.7×10^9/l
PLT	263×10^9/l

Reticulocytes	145 × 10^9/l
Blood film	Macrophages with ingested erythrocytes
Creatinine	195 µmol/l
Direct Coomb's test at room temperature	-

What is the most likely diagnosis?

A	Cold haemagglutinin disease
B	Paroxysmal cold haemoglobinuria
C	Rhabdomyolysis
D	Paroxysmal nocturnal haemoglobinuria
E	Evan's syndrome

Question 18 of 60

An 18-year-old man presents to the Accident and Emergency Department with severe back pain that came on while he was ice-skating. He has recently recovered from a viral upper respiratory tract infection, but is otherwise fit and well. He developed back pain without any obvious trauma, and passed dark red urine: he has not passed urine since (four hours ago). He is on no medications and does not smoke or drink. There is no family history of note.

On examination, he is in severe discomfort, temperature 38.3 °C, pulse 120 beats per minute, blood pressure 145/83 mmHg, peripheries are well perfused and there is no cyanosis. He is icteric. Abdominal, respiratory and cardiovascular examinations are unremarkable.

Investigations:

Hb	8.3 g/dl
WCC	4.7×10^9/l

B Paroxysmal cold haemoglobinuria

This patient has developed acute intravascular haemolysis (anaemia, high reticulocyte count, jaundice, haemoglobinuria) in response to cold exposure. In PCH, an antibody that binds temporarily in the cold develops in response to infection – classically syphilis, but more commonly various viral infections including Epstein–Barr virus – and on warming, dissociates and activates complement, causing rapid intravascular haemolysis, with rigors and severe bone pain. The antibody is to the P blood group, and is confirmed by the finding of a Donath-Landsteiner antibody – the patient's serum is incubated with red blood cells at 4°C and warmed, with subsequent haemolysis. P-negative blood (pp) can be used as a negative control. The Coombs test, now more appropriately called the direct agglutination test, is often negative, particularly if taken some time after the episode. It is more likely to be positive if samples are tested at an

positive if samples are tested at an appropriate temperature. Kidney disease can ensue, but patients in general have a single episode that responds to supportive care.

D	Paroxysmal nocturnal haemoglobinuria

PNH is associated with repeated complement-mediated haemolysis and presents with more marked urinary discoloration in the morning.

A	Cold haemagglutinin disease

Cold haemagglutinin disease is not usually paroxysmal in nature, and the Coombs test is positive for C3d: the blood film usually shows agglutination of red cells. Taking these factors together, cold haemagglutinin disease is incorrect.

C	Rhabdomyolysis

Rhabdomyolysis is associated with

A Cold haemagglutinin disease

Cold haemagglutinin disease is not usually paroxysmal in nature, and the Coombs test is positive for C3d: the blood film usually shows agglutination of red cells. Taking these factors together, cold haemagglutinin disease is incorrect.

C Rhabdomyolysis

Rhabdomyolysis is associated with significant muscle necrosis and also with trauma, although none has been described here.

E Evan’s syndrome

Evans is Coombs-positive autoimmune haemolytic anaemia, a rare condition of unknown aetiology.

6305

C Thoracoplasty

This question is a 'spot diagnosis'. Clues that this is a thoracoplasty and not any of the alternative options are that there is evidence of rib resection in conjunction with loss of lung volume. The CXR shows a thoracoplasty. This lady had tuberculosis in the 1940s, prior to the use of anti-tuberculosis chemotherapy. She had a thoracoplasty, which was one of the main surgical treatments for tuberculosis between 1930 and 1955. Several ribs were resected, which reduced the thoracic volume and collapsed the underlying lung. The aim was to close the tuberculous cavity and 'rest the lung'. Control of pulmonary tuberculosis and survival was good. However, patients were left with severe chest deformity and the associated respiratory compromise, a restrictive defect.

B Left pneumonectomy

A 28-year-old woman is admitted to the ward from the Gastroenterology Clinic. She has ulcerative colitis which is usually quiescent, but despite maximal mesalazine and prednisolone 60 mg daily she is opening her bowels some 8–10 times per day with bloody diarrhoea.

You examine her on the ward; her BP is 110/70 mmHg, pulse 92/min. Her temperature is 37.8 °C.

On examination, her abdomen is distended and tender, with sparse bowel sounds. Her right leg is also swollen.

Investigations:

Hb	10.0 g/dl
WCC	10.2×10^9/l
PLT	130×10^9/l
CRP	72 mg/l
Na^+	139 mmol/l
K^+	3.8 mmol/l

K^+	3.8 mmol/l
Creatinine	110 µmol/l
Abdominal X-ray	Dilated left-sided colon with evidence of mucosal oedema
Right leg venogram	Above-knee deep venous thrombosis (DVT)

Which of the following is the most appropriate way to manage her DVT?

A	Clopidogrel and aspirin
B	Elastic stockings
C	Rivaroxaban
D	Fondaparinux
E	Unfractionated heparin

20948

Question 1 of 42

CRP	72 mg/l
Na^+	139 mmol/l
K^+	3.8 mmol/l
Creatinine	110 µmol/l
Abdominal X-ray	Dilated left-sided colon with evidence of mucosal oedema
Right leg venogram	Above-knee deep venous thrombosis (DVT)

Which of the following is the most appropriate way to manage her DVT?

Your answer was correct

A	Clopidogrel and aspirin
B	Elastic stockings
C	Rivaroxaban

Question 1 of 42

E Unfractionated heparin

Patients with an exacerbation of ulcerative colitis are at greatly increased risk of thromboembolic disease. This patient has an extensive right-sided DVT and is at significant risk of developing a pulmonary embolus. Heparinisation is the most appropriate intervention, which can be reversed in the event that surgery is required.

A Clopidogrel and aspirin

Dual anti-platelet therapy neither prevents DVT nor impacts on its progression, and it is therefore not an appropriate intervention here.

B Elastic stockings

Although stockings may be considered for prophylaxis, they aren't appropriate as treatment for an above-knee DVT.

C Rivaroxaban

B Elastic stockings

Although stockings may be considered for prophylaxis, they aren’t appropriate as treatment for an above-knee DVT.

C Rivaroxaban

Rivaroxaban is a factor X inhibitor. Although it is useful as a long-term intervention for anti-coagulation in AF or venous thromboembolism, it cannot easily be reversed if surgery is required.

D Fondaparinux

Fondaparinux is a factor Xa inhibitor primarily used in the treatment of acute coronary syndrome.

20948

An 84-year old man presents with easy bruising of 3 months' duration. He was previously fit and well, but has lost a stone in weight recently. He is on no medication and has no allergies. Direct questioning is unremarkable other than some symptoms of prostatism.

Examination shows him to be icteric, with multiple bruises. Abdomen is soft and non-tender with no abnormal masses.

Investigations:

Hb	8.0 g/dl
WCC	13.7 × 10^9/l
PLT	56 × 10^9/l
Activated PTT	48 s (30-40)
Fibrinigen	0.9 g/l (1.8-5.4)
Bilirubin	35 μmol/l
Blood film	Schistocytes, nucleated red blood cells, metamyelocytes and myelocytes

Question 2 of 42

Blood film	Schistocytes, nucleated red blood cells, metamyelocytes and myelocytes
Na^+	139 mmol/l
K^+	4.5 mmol/l
Creatinine	167 µmol/l (up from 138 some 6 months earlier)

What is the most likely diagnosis?

A	Prostate cancer
B	Chronic myeloid leukaemia (CML)
C	Myelofibrosis
D	Thrombotic thrombocytopenic purpura
E	Haemolytic uraemic syndrome

A Prostate cancer

This elderly man has evidence of disseminated intravascular coagulation (DIC) – abnormal clotting, low fibrinogen and low platelets – with an associated microangiopathic haemolytic anaemia (MAHA) – schistocytes, also known as fragmented red cells. The commonest cause of chronic DIC in an elderly man with prostatic symptoms is prostate cancer: the presence of immature red (nucleated red blood cells) and white (metamyelocytes and myelocytes) cells in the blood is known as a leucoerythroblastic blood film, and is often seen in cases of bone marrow invasion (and is relatively frequently present in metastatic prostatic cancer, particularly hormone-resistant cases). The diagnosis could be confirmed by measuring prostatic-specific antigen and taking a bone marrow trephine, which may show marrow invasion by gland-forming metastases.

B Chronic myeloid leukaemia

CML most often presents in the 4th and 5th decades. In more than half of patients with CML, the spleen extends more than 5 cm below the left costal margin at the time of discovery. Peripheral blood findings in CML show a typical leukoerythroblastic blood picture, with circulating immature cells from the bone marrow.

C Myelofibrosis

Like CML, myelofibrosis is commonly associated with splenomegaly, and symptoms of prostatism with evidence of haemolysis would not be expected.

D Thrombotic thrombocytopenic purpura

TTP can cause MAHA, but does not lead to elevation in APTT, and is associated with cerebral infarction.

E Haemolytic uraemic syndrome

A 50-year-old white man is referred by his general practitioner (GP) with cellulitis of his right leg that has been difficult to treat with oral antibiotics. The patient has been experiencing increased fatigue and breathlessness. He drinks a glass of wine at the weekends and is a non-smoker. Apart from childhood asthma, he is well and on no regular medication.

On examination: Pale conjunctivae and multiple bruises over all four limbs. There is hepatosplenomegaly and cellulitis of right leg.

Investigations:

Hb	8.2 g/dl
WBC	3×10^9/l
PLT	95×10^9/l
MCV	83 fl
Bone marrow aspirate	Dry tap
Bone marrow biopsy	Cells with a 'fried egg' appearance

Question 3 of 42

Bone marrow aspirate	Dry tap
Bone marrow biopsy	Cells with a 'fried egg' appearance
Tartrate-resistant acid phosphatase stain (TRAP)	strongly positive

What is the most likely diagnosis?

A Chronic myeloid leukaemia

B Hairy cell leukaemia

C Myelodysplasia

D Myelofibrosis

E Chronic lymphocytic leukaemia

7067

12:51

Question 3 of 42

Hb	8.2 g/dl
WBC	3 x 10^9/l
PLT	95 x 10^9/l
MCV	83 fl
Bone marrow aspirate	Dry tap
Bone marrow biopsy	Cells with a 'fried egg' appearance
Tartrate-resistant acid phosphatase stain (TRAP)	strongly positive

What is the most likely diagnosis?

Your answer was incorrect

A Chronic myeloid leukaemia

B Hairy cell leukaemia

C Myelodysplasia

B Hairy cell leukaemia

Hairy cell leukaemia is a β-lymphocyte disorder. The abnormal cell has hair-like cytoplasmic projections. Infiltration of the bone marrow leads to pancytopenia and patients have hepatosplenomegaly. The abnormal cells are strongly positive for tartrate-resistant acid phosphatase stain (TRAP). Infiltration of the bone marrow gives a dry tap, and a bone marrow biopsy reveals cells that are said to have the characteristic 'fried egg' appearance. Purine analogues and interferon have been used for treatment, and occasionally splenectomy has been required.

Stains:

- TRAP: tends to be positive in hairy cell leukaemia
- Sudan black B stain and myeloperoxidase: tends to be positive in acute myeloblastic leukaemia
- Terminal deoxynucleotidyl

- Terminal deoxynucleotidyl transferase stain (TDT): tends to be positive in acute lymphoblastic leukaemia
- LAP: tends to be raised in polycythemia rubra vera and myelofibrosis; tends to be low in chronic myeloid leukaemia.

D **Myelofibrosis**

Primary myelofibrosis (PMF) is one of the chronic myeloproliferative disorders, which are collectively characterised by clonal proliferation of myeloid cells with variable morphologic maturity and haematopoietic efficiency. Splenomegaly is a marked feature. Bone marrow biopsy is necessary to demonstrate fibrosis. Some degree of fibrosis is seen in almost all patients; the fibrosis is typically extensive and visualised better with a silver stain (reticulin) or a trichrome stain (mature collagen). Bone marrow sinusoids are

collagen). Bone marrow sinusoids are expanded and there is intravascular haematopoiesis. The fibrosis is generally associated with atypical megakaryocytic hyperplasia, and thickening and distortion of the bony trabeculae (osteosclerosis).

A Chronic myeloid leukaemia

CML is a myeloproliferative disorder characterised by the proliferation of the precursors for white blood cells, but these precursors retain the ability to differentiate. Symptoms tend to be chronic and the blood profile shows an increased (++) white cell count, with a low or normal haemoglobin and a variable platelet count.

C Myelodysplasia

Myelodysplasia occurs mainly in the elderly and presents with anaemia, infection or bleeding due to pancytopenia. Serial blood counts show evidence of increasing bone marrow failure and the bone marrow

marrow failure and the bone marrow shows increased cellularity. Patients with <5% blasts in the bone marrow are managed conservatively, ‘gentle’ chemotherapy is used in patients with high white blood cell counts and intensive chemotherapy is usually reserved for patients under the age of 60 years. Transformation into AML occurs in around 30% of patients. Bone marrow biopsy revealing cells that are said to have the characteristic ‘fried egg’ appearance is characteristic of hairy cell leukaemia.

E	Chronic lymphocytic leukaemia

The most noteworthy laboratory abnormality found in CLL is lymphocytosis in the peripheral blood and bone marrow. Although the absolute blood lymphocyte threshold for diagnosing CLL has been placed at >5000/microl (5 × 109/l) B lymphocytes, a significant proportion of patients presents with counts as high as 100,000/microl (100 × 109/l). The peripheral blood smear of patients

The most noteworthy laboratory abnormality found in CLL is lymphocytosis in the peripheral blood and bone marrow. Although the absolute blood lymphocyte threshold for diagnosing CLL has been placed at >5000/microl (5 × 109/l) B lymphocytes, a significant proportion of patients presents with counts as high as 100,000/microl (100 × 109/l). The peripheral blood smear of patients with CLL demonstrates a lymphocytosis. The leukemic cells are typically small, mature-appearing lymphocytes with a dense nucleus, partially aggregated (clumped) chromatin and lacking discernible nucleoli. There is a narrow border of clear to slightly basophilic cytoplasm. The blood film in this scenario is not that of CLL. Bone marrow biopsy revealing cells that are said to have the characteristic ‘fried egg’ appearance’ is characteristic of hairy cell leukaemia, and therefore CLL is an incorrect option.

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You are asked to counsel a married couple expecting a baby. They are both fit and well, with no previous medical history.

They both originate from South East Asia, and have no family history of birth abnormalities. There are no abnormalities on examination.

Investigations:

MALE

Hb	11.7 g/dl
Mean cell volume	70 fl (80-96)
Mean cell haemoglobin	19 pg (27-33)
Red cell count	5.6 x 10^{12}/l (4.7-6.9)
Haemoglobin electrophoresis	normal

FEMALE

Hb	10.1 g/dl
Mean cell volume	68 fl

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FEMALE

Hb	10.1 g/dl
Mean cell volume	68 fl
Mean cell haemoglobin	18 pg
Red cell count	6.0 x 10^{12}/l
Haemoglobin electrophoresis	normal

What condition is the fetus at risk from inheriting?

A	ß-Thalassaemia trait
B	Thalassaemia intermedia
C	Hydrops fetalis
D	β -Thalassaemia major
E	Homozygous haemoglobin E

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C Hydrops fetalis

Both patients come from an area endemic for a-thalassaemia, and appear to be carriers, with high red blood cell counts and hypochromia/microcytosis. Hydrops fetalis is associated with homozygous alpha-thalassaemia, thus driving the correct answer.

B Thalassaemia intermedia

The terms thalassaemia minor, intermedia and major do not pertain to a- or β-thalassaemia - rather they describe whether the patient is asymptomatic (minor), transfusion dependent (major) or in between (intermedia). Loss of a single a chain (aa/–a) is common (30% in Africa); loss of two a chains (aa/––) is less common, and co-inheritance can lead to hydrops fetalis (––/––), where no a chains are produced, and haemoglobin (Hb) Barts is produced (a gamma-4 tetramer). Loss of three alpha chains

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tetramer). Loss of three alpha chains (a-/--) leads to haemoglobin H (HbH) disease (HbH is composed of beta-4 tetramers), usually with a thalassaemia intermedia phenotype.

A ß-Thalassaemia trait

Patients with β-thalassaemia trait nearly always have a raised haemoglobin A2 and fetal haemoglobin on haemoglobin electrophoresis (although normal A2 variants do exist). The fact that both parents have normal haemoglobin electrophoresis means there is effectively very low/no significant risk of the fetus inheriting beta-thalassaemia trait.

D β -Thalassaemia major

β-Thalassaemia trait in the parents has effectively been ruled out by the normal haemoglobin electrophoresis, and therefore β-thalassaemia won't occur in the fetus in this case.

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haemoglobin on haemoglobin electrophoresis (although normal A2 variants do exist). The fact that both parents have normal haemoglobin electrophoresis means there is effectively very low/no significant risk of the fetus inheriting beta-thalassaemia trait.

D β -Thalassaemia major

β-Thalassaemia trait in the parents has effectively been ruled out by the normal haemoglobin electrophoresis, and therefore β-thalassaemia won't occur in the fetus in this case.

E Homozygous haemoglobin E

Haemoglobin-E is associated with mild β-thalassaemia which presents in the first few months of life, and isn't usually a cause of fetal loss.

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A 65-year-old gentleman presented to the Emergency Department with persistent nose and gum bleeding. He had also noticed some blurred vision and frontal headaches over the past few hours.

On examination, he was pale and only his gums were actively bleeding. Neurological examination revealed bilateral horizontal nystagmus on left lateral gaze. Ophthalmic examination revealed bilateral decreased visual acuity and retinal haemorrhages.

Investigations:

Hb	9.1 g/dl
WCC	8 × 10^9/l
PLT	130 × 10^9/l
Urea	10 mmol/l
Creatinine	170 µmol/l
Corrected calcium	2.8 mmol/l
Phosphate	1.77 mmol/l
Total protein	89 g/dl

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Phosphate	1.77 mmol/l
Total protein	89 g/dl
Albumin	30 g/dl
PT	16 s (10–13 seconds)
APTT	55 s (20–35 s)
Peripheral blood smear	Rouleaux formation

What is the most likely cause for his presentation?

A	Hypercalcaemia
B	Bernard–Soulier syndrome
C	Glanzmann thrombasthenia
D	Hyperviscosity syndrome
E	Acute kidney disease

On examination, he was pale and only his gums were actively bleeding. Neurological examination revealed bilateral horizontal nystagmus on left lateral gaze. Ophthalmic examination revealed bilateral decreased visual acuity and retinal haemorrhages.

Investigations:

Hb	9.1 g/dl
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Total protein	89 g/dl
Albumin	30 g/dl
PT	16 s (10–13 seconds)

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D	Hyperviscosity syndrome

Hyperviscosity syndrome (HSV) refers to the clinical sequelae of increased blood viscosity. Increased serum viscosity usually results from increased circulating serum immunoglobulins, and can be seen in such diseases as Waldenström macroglobulinaemia and multiple myeloma. HVS can also result from increased cellular blood components (typically white or red blood cells) in hyperproliferative states such as the leukaemias, polycythaemia and the myeloproliferative disorders. The clinical presentation in HVS consists principally of the triad of mucosal bleeding, visual changes and neurologic symptoms. Plasmapheresis is the treatment of choice. This removes the circulating paraproteins and reduces the viscosity.

A	Hypercalcaemia

The neurological symptoms and gum bleeding do not correspond to the clinical presentation of hypercalcaemia

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clinical presentation of hypercalcaemia (lack of concentration, feeling of ‘pins and needles’).

B	Bernard–Soulier syndrome

This is caused by a deficiency on the surface of the platelet of the glycoprotein Ib/IX receptor that results in a failure of platelets to stick together in a clump at the site of an injury.

C	Glanzmann thrombasthenia

This results in a deficiency in platelet adhesion as a consequence of a deficiency of the surface protein glycoprotein IIb/IIIa.

E	Acute kidney disease

Uraemic encephalopathy would not cause the neurological symptoms described in this scenario. Acute kidney disease usually presents with

A 32-year-old woman presents with increasing breathlessness and angina pain.

Examination reveals pale conjunctivae. She has evidence of a left lower lobe consolidation on auscultation of the chest. Petechiae are present on the lower limbs.

Observations:

Blood pressure	125/79 mmHg
Heart rate	100 bpm, regular
Temperature	37.9 °C
Oxygen saturations	94% on air

Investigations:

Haemoglobin (Hb)	7.5 g/dl
White blood cells (WBC)	2.5 × 10⁹/l
Platelets (PLT)	23 × 10⁹/l

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Haemoglobin (Hb)	7.5 g/dl
White blood cells (WBC)	2.5 × 10^9/l
Platelets (PLT)	23 × 10^9/l
Blood film	Blast cells with Auer rods

Given the likely clinical diagnosis, what feature is most associated with a negative outlook?

A Low total WBC count

B Translocation t(8:21)

[✓ C] Deletion of part of chromosome 5, (5q-)

D Age 32

E Platelet count of 23

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C Deletion of part of chromosome 5, (5q-)

With the diagnosis being acute myeloid leukaemia (AML), there are a number of abnormalities which are considered unfavourable when they occur in cases that do not also contain favourable karyotypic changes; these include del (5q-); add (5q+); del (7q-); add (7q+); monosomies of chromosome 5 or 7 and other more complex translocations and additions are also associated with a poor outlook.

A Low total WBC count

Although a low total WBC count may be associated with an increased risk of infection at initial presentation, it does not significantly impact on prognosis vs other abnormalities such as changes in karyotype.

B Translocation t(8:21)

B Translocation t(8:21)

A number of favourable karyotype abnormalities exist in AML; these include t(8;21), inv(16)(p13;q22), t(16;16)(p13;q22) and t(15;17)(q24.1;q21.1), which identifies acute promyelocytic leukaemia.

D Age 32

Survival in AML deteriorates significantly at age 40 and above, with survival at age 60 or greater falling to 13% or lower.

E Platelet count of 23

Thrombocytopenia is commonly observed in patients with AML and does not significantly impact prognosis vs other factors such as renal impairment, performance status, prior haematological malignancy and karyotype abnormalities.

A confused 68-year-old man was brought to the Emergency Department with a 3-day history of severe headaches, blurred vision and spontaneous gum bleeding. Prior to his acute presentation, he had been generally unwell for several months with malaise and weight loss.

On examination, he was drowsy and had widespread lymphadenopathy and a palpable spleen. Heart sounds were normal and his chest was clear to auscultation. Ophthalmoscopy revealed several retinal haemorrhages. There were no focal neurological signs.

Investigations:

Hb	10.0 g/dl
WCC	3.5 × 10^9/l
PLT	130 × 10^9/l
Na^+	135 mmol/l
K^+	4.2 mmol/l
Creatinine	170 µmol/l

MCV	96 fl
Urea	7.2 mmol/l
ESR	90 mm/h
Blood film	Rouleaux formation

Serum immunoglobulins:

IgA	3.5 g/l (0.5–4.0)
IgG	10.0 g/l (5.0–13.0)
IgM	22.0 g/l (0.3–2.2)

What is the most likely diagnosis?

A	Tuberculous meningitis
B	Multiple myeloma
C	Herpes simplex encephalitis
D	Waldenstrom’s macroglobulinaemia

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ESR	90 mm/h
Blood film	Rouleaux formation

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What is the most likely diagnosis?

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C	Herpes simplex encephalitis
D	Waldenstrom's macroglobulinaemia
E	Chronic lymphocytic leukaemia

D Waldenstrom's macroglobulinaemia

This man has a hyperviscosity syndrome, which occurs when the plasma viscosity rises to a level at which the micro-circulation is impaired (typically >5). Waldenstrom's macroglobulinaemia is the most common cause of this. Waldenstrom's is a lymphoplasmacytoid malignancy, which tends to occur in older men. There is a recently identified genetic component with a high percentage of patients carrying the *MYD88* gene. It usually presents with peripheral lymph node enlargement, enlarged spleen and symptoms of bone marrow infiltration, and is associated with an IgM paraprotein. The high circulating levels of IgM paraprotein form aggregates therefore increase the viscosity of the blood, leading to hyperviscosity syndrome.

Criteria for diagnosis of Waldenström's macroglobulinemia (WM) include:

1. IgM monoclonal gammopathy that

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Criteria for diagnosis of Waldenström's macroglobulinemia (WM) include:

1. IgM monoclonal gammopathy that excludes chronic lymphocytic leukaemia and Mantle cell lymphoma
2. Evidence of anaemia, systemic symptoms, hyperviscosity, enlarged lymph nodes or hepatomegaly orand/or splenomegaly that can be attributed to an underlying lymphoproliferative disorder.

Treatment is with alkylating agents or doxorubicin-containing regimes. Plasmapheresis is used for hyperviscosity due to IgM levels.

Less common causes include myeloma (immunoglobulin A (IgA) or IgM paraprotein), polycythaemia or leukaemia (leucostasis).

A	Tuberculous meningitis

This patient has no history of exposure to tuberculosis. TB meningitis is

This is the family tree of a family affected with haemophilia A (males denoted by squares, females denoted by circles).

What are the chances of ‘M’ being affected?

A 1 in 1

B 1 in 2

C 1 in 3

D 1 in 4

E 1 in 6

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B 1 in 2

Haemophilia A is a sex-linked inherited disease in humans. Males are hemizygous and receive their only X chromosome from their mother. Females are heterozygous and receive one X chromosome from each parent. Consequently, if a male has an affected X chromosome, he will be affected by an X-linked disease. In the above family tree, the daughter of the affected individual will receive the diseased X chromosome from her father and a normal X chromosome from her mother, so that she is a carrier of the disease. Her son, in turn, will have a 1 in 2 chance of receiving the diseased chromosome from his carrier mother, so the chance of him being affected with haemophilia A is 1 in 2.

E 1 in 6

1 in 6 doesn't fit with a pattern of Mendelian inheritance.

A 70-year-old man presents with recurrent chest infections and abdominal discomfort. He was well until a year ago, but has required recurrent courses of antibiotics from his general practitioner (GP) for chest infections. He has discomfort in the left upper part of his abdomen, and finds that he feels full despite eating only a few mouthfuls at each meal.

On examination, he has a large spleen, palpable 10 cm below the costal margin.

Investigations:

Hb	8.7 g/dl
WCC	23.2 × 10⁹/l
Platelets	25 × 10⁹/l
Neutrophils	0.3 × 10⁹/l
Monocytes	-
Lymphocytes	21 × 10⁹/l
	Large numbers of atypical monocytes with abnormal villous

Lymphocytes	21 × 10^9/l
Blood film	Large numbers of atypical monocytes with abnormal villous projections (not picked up on the automated count)

Which of the following is the most likely diagnosis?

A Chronic lymphocytic leukaemia

B Infectious mononucleosis

C Splenic lymphoma with villous lymphocytes

D Pro-lymphocytic leukaemia

E Hairy cell leukaemia

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E	Hairy cell leukaemia

This gentleman has anaemia, thrombocytopenia, massive splenomegaly and monocytopenia – the last of these is classic for hairy cell leukaemia, and the diagnosis is confirmed by the morphological appearances on the blood film. The typical hairy cells are named because of their characteristic cytoplasmic projections, which appear as fine (hair-like) microvilli when seen by light microscopy, phase-contrast and electron microscopy. These are abnormal B-lymphocyte cells with eccentric or centrally placed nuclei. Hairy cell leukaemia responds dramatically to the purine analogues cladribine and pentostatin, with resulting survival rates at five years of 95–98%.

A	Chronic lymphocytic leukaemia

CLL can often be picked up on routine blood tests. It often presents

blood tests. It often presents asymptomatically, but sometimes patients have splenomegaly or enlarged lymph nodes. Smudge cells and abnormal B-lymphocytes (without villous projections) are seen on a blood film.

B	Infectious mononucleosis

This is caused by Epstein–Barr Virus (EBV), and a positive monospot test is diagnostic. There is an increase in lymphocytes on full blood count. It tends to affect a younger population.

C	Splenic lymphoma with villous lymphocytes

This condition is extremely rare. This patient's blood film shows villous projections on monocytes, not lymphocytes, and it does not cause monocytopenia.

D	Pro-lymphocytic leukaemia

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A 70-year-old man presents with worsening headaches, three TIAs in the past 6 months and exertional angina. He is a smoker of 30 cigarettes per day and has a history of hypertension for which he takes ramipril 10 mg daily.

On examination, his BP is 165/90 mmHg and he looks plethoric.

Investigations:

Hb	18.5 g/dl
WCC	$14.1 \times 10^9/l$
PLT	$520 \times 10^9/l$
K^+	5.4 mmol/l
Creatinine	160 µmol/l

Which of the following results of further investigations is most likely to differentiate between primary and secondary polycythaemia?

A	Hypoxia on arterial blood gas testing

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PLT	520 x 10^9/l
K^+	5.4 mmol/l
Creatinine	160 µmol/l

Which of the following results of further investigations is most likely to differentiate between primary and secondary polycythaemia?

A	Hypoxia on arterial blood gas testing
B	Hypercapnia on arterial blood gas testing
C	Low erythropoietin
D	Elevated CO levels
E	Raised viscosity

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C	Low erythropoietin

Patients with primary polycythaemia carry a mutation that leads to hypersensitivity to erythropoietin. As such, even in the presence of low erythropoietin levels there is a drive to produce more red blood cells. The symptoms seen here are due to increased red cell mass, consequent increase in plasma volume and raised plasma viscosity.
An activating mutation in JAK2 is identified in many patients diagnosed with primary polycythaemia; this induces EPO hypersensitivity. Eventual transformation of primary polycythaemia may occur to acute myeloid leukaemia, chronic lymphocytic leukaemia or chronic myeloid leukaemia.

A	Hypoxia on arterial blood gas testing

Chronic hypoxia can cause secondary polycythaemia. This can be due to various conditions such as respiratory

various conditions such as respiratory diseases (COPD, asthma) or cardiac causes (heart failure). It is not a marker used to differentiate between primary and secondary polycythaemia.

B Hypercapnia on arterial blood gas testing

Hypercapnia is a marker of respiratory conditions such as COPD. Again, this will lead to secondary polycythaemia with raised erythropoietin levels.

D Elevated CO levels

These are elevated in carbon monoxide poisoning. Elevated CO levels of at least 3–4% in non-smokers and at least 10% in smokers are significant. Diagnosis is confirmed by demonstrating an elevated level of carboxyhaemoglobin (HbCO).

E Raised viscosity

This is not a specific test and can be

conditions such as COPD. Again, this will lead to secondary polycythaemia with raised erythropoietin levels.

D	Elevated CO levels

These are elevated in carbon monoxide poisoning. Elevated CO levels of at least 3–4% in non-smokers and at least 10% in smokers are significant. Diagnosis is confirmed by demonstrating an elevated level of carboxyhaemoglobin (HbCO).

E	Raised viscosity

This is not a specific test and can be raised in inflammatory, infectious and autoimmune conditions.

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A 70-year-old man presents unconscious to the Accident and Emergency Department. He had been found at his sheltered accommodation by the warden, who brought in his medications: warfarin, furosemide and amoxycillin (10-day course, 5 days' used).

Examination showed a Glasgow coma scale of 5/15, a dilated left-sided pupil and right-sided upper motor neurone signs in the upper and lower limbs. A computed tomography scan of the brain shows a large, left-sided subdural haematoma. Ten milligrams intravenous vitamin K was given immediately.

Investigations:

Hb	9.5 g/dl
WCC	5.3 x 10^9/l
PLT	403 x 10^9/l
APTT	43 s (30–40s)
INR	7.0 (target INR 2.5)

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WCC	5.3 x 10^9/l
PLT	403 x 10^9/l
APTT	43 s (30–40s)
INR	7.0 (target INR 2.5)

What is the best way to reverse his warfarin?

A	Prothrombin complex concentrate up to 3000U according to body weight
B	Fresh frozen plasma 15 ml/kg stat
C	Factor VIII bypassing agent (FEIBA)
D	Ten units of cryoprecipitate
E	IV vitamin K

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A	Prothrombin complex concentrate up to 3000U according to body weight

Prothrombin complex concentrate contains the vitamin K-dependent factors and normalises clotting within minutes of administration; it is the recommended product for life-threatening bleeding due to over-anticoagulation with warfarin. It is plasma derived, so there is a potential risk of transfusion-transmitted infection, and it is prothrombotic.

B	Fresh frozen plasma 15 ml/kg stat

Fresh frozen plasma (FFP) contains low levels of coagulation factors and it is estimated that even at a dose of 15 ml/kg, levels of most factors will only approach 20% of normal. In addition, the large volumes of FFP required are likely to precipitate pulmonary oedema, particularly in an elderly man on furosemide. It is only really considered if other options such as

on furosemide. It is only really considered if other options such as PCC are not available.

C	Factor VIII bypassing agent (FEIBA)

FEIBA contains activated factors II, VII, IX and X and is highly thrombogenic; its main use is in the management of acquired inhibitors in haemophilia.

D	Ten units of cryoprecipitate

Cryoprecipitate contains predominantly fibrinogen and factor VIII and it is therefore less effective in reversing bleeding due to warfarin versus PCC.

E	IV vitamin K

Vitamin K given intravenously will start to affect the INR for prothrombin activity within 4–8 h, but this patient is showing signs of temporal lobe herniation (ipsilateral fixed and dilated

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D Ten units of cryoprecipitate

Cryoprecipitate contains predominantly fibrinogen and factor VIII and it is therefore less effective in reversing bleeding due to warfarin versus PCC.

E IV vitamin K

Vitamin K given intravenously will start to affect the INR for prothrombin activity within 4–8 h, but this patient is showing signs of temporal lobe herniation (ipsilateral fixed and dilated pupil) and needs immediate cessation of bleeding if he is to survive.

A 30-year-old woman presents with a 3-week history of easy bruising and menorrhagia. On the day of presentation, she developed ‘heaviness’ in her left arm and slurred speech. She is taking tranexamic acid, prescribed for the menorrhagia. She has no previous medical history of note. According to her husband she was incoherent and confused for half an hour. She is seen in casualty and is conversing easily.

Examination shows a Glasgow coma scale of 15/15, normal neurological examination and normal speech. Temperature is 37.5 °C, pulse is 105 beats per minute (bpm), blood pressure is 130/70 mmHg and heart sounds are normal. She has several bruises on her shins and forearms. A computed tomography (CT) scan of the brain is normal.

Investigations:

Hb	8.5 g/dl
PLT	17 x 10^9/l

MCV	102 fl
Reticulocytes	130 x 10^9/l (25–85)
LDH	735 U/l (10–250)
Blood film	Low counts, numerous schistocytes
PT	15 s (11.5–15.5)
APTT	33 s (30–40)
Pregnancy test	-

Her tranexamic acid is stopped.

Which of the following is the most appropriate intervention?

A Plasmapheresis

B Clopidogrel 75 mg

C Aspirin 75 mg

Blood film	Low counts, numerous schistocytes
PT	15 s (11.5–15.5)
APTT	33 s (30–40)
Pregnancy test	-

Her tranexamic acid is stopped.

Which of the following is the most appropriate intervention?

A Plasmapheresis

B Clopidogrel 75 mg

C Aspirin 75 mg

D Platelet transfusion

E Epsilon aminocaproic acid

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A Plasmapheresis

The results show anaemia with a raised reticulocyte count and lactate dehydrogenase, implying haemolysis, and the presence of schistocytes is most compatible with a micro-angiopathic mechanism. Coupled with low platelets and fluctuating neurological signs, this is classical for thrombotic thrombocytopenic purpurae (TTP). The treatment for this is urgent plasmapheresis with fresh frozen plasma or cryosupernate, which is thought to significantly reduce mortality, although there is an absence of randomised controlled trials in this area. In this patient the tranexamic acid is prothrombotic and may be worsening the condition, and hence it has been stopped. Eculizumab may also be utilised in patients with refractory TTP.

The condition is caused by an acquired auto-antibody to a metalloproteinase ADAMTS13, the function of which is to control the size of von Willebrand's

ADAMTS13, the function of which is to control the size of von Willebrand's factor multimers. As a result, ultra-large von Willebrand's factor multimers, with enhanced activity, accumulate and cause increased binding of platelets to small blood vessels. The platelet count falls and red cells are damaged when they pass through the narrowed vessels, causing micro-angiopathy. It is not clear why the brain is the main organ affected in TTP compared with the kidney in the related condition haemolytic uraemic syndrome.

B	Clopidogrel 75 mg

Case reports of TTP occurring in association with clopidogrel therapy exist, although it is sometimes used in patients with TTP once the platelet count reaches >50, in the event that the patient is unable to take aspirin.

C	Aspirin 75 mg

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association with clopidogrel therapy exist, although it is sometimes used in patients with TTP once the platelet count reaches >50, in the event that the patient is unable to take aspirin.

C	Aspirin 75 mg

Aspirin is only used on the context of TTP once the platelet count reaches >50.

D	Platelet transfusion

Platelet transfusion is not recommended in patients with TTP, and it may actually have a negative impact on outcomes.

E	Epsilon aminocaproic acid

Epsilon aminocaproic acid is used as a treatment for acute haemorrhage, but is not in the treatment of TTP.

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An 18-year-old Greek woman with beta-thalassaemia major, and who has had several blood transfusions and uses desferrioxamine for prevention of iron overload, comes to the clinic with her sister who is 25 years old and wants to start a family.

They want to discuss the mutation that is the basis of the 18-year old's underlying disease.

Which of the following is the basis of beta-thalassaemia major?

A 1 alpha-chain gene mutation

B 1 beta-chain gene mutation

C 2 alpha-chain gene mutations

D 1 alpha- and one beta-chain gene mutation

E 2 beta-chain mutations

E 2 beta-chain mutations

Beta-thalassaemia major is due to mutations in the genes coding for each of the beta-globin chains. This results in grossly ineffective erythropoiesis and severe hypochromic microcytic anaemia with iron overload. The profound anaemia is associated with erythroid hyperplasia and extramedullary haemopoiesis. Given that her parents were unaffected by thalassaemia major but must have suffered from the thalassaemia trait, the 25-year-old sister has a 66% chance of having the thalassaemia trait, (she is symptomless, meaning that she must either be normal or carry a mutation for 1 of the 2 beta-globin genes). She should be advised to have haemoglobin electrophoresis prior to beginning a family with her new partner.

A 1 alpha-chain gene mutation

One alpha-chain mutation leads to so-

called silent alpha-thalassaemia, which is asymptomatic.

B 1 beta-chain gene mutation

This leads to beta-thalassaemia trait, which is the likely diagnosis in the 25-year-old sibling of the patient with thalassaemia major.

C 2 alpha-chain gene mutations

Two alpha-chain mutations lead to alpha-thalassaemia trait microcytic anaemia, which is usually asymptomatic.

D 1 alpha- and one beta-chain gene mutation

Mixed alpha- and beta-thalassaemia is said to carry a milder clinical course than thalassaemia major.

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A 53-year-old man presents with tiredness of 3 months' duration. He has had abdominal pains in the past year that are fleeting in nature, and he has lost one stone in weight. He is on antacids and has no significant previous medical history.

On examination, he is slim with pale conjunctivae, but otherwise there is nothing abnormal to find.

Investigations:

Hb	5.5 g/dl
WCC	4.3 x 10^9/l
PLT	523 x 10^9/l
Ferritin	5 µg/l (15–300)
Calcium	2.05 mmol/l

Colonoscopy and gastroscopy are normal (although gastroscopy was abandoned before biopsies were taken due to patient discomfort).

Which investigation would be most useful in making a diagnosis?

Ferritin	5 µg/l (15–300)
Calcium	2.05 mmol/l

Colonoscopy and gastroscopy are normal (although gastroscopy was abandoned before biopsies were taken due to patient discomfort).

Which investigation would be most useful in making a diagnosis?

A	Repeat colonoscopy and gastroscopy
B	Isotope-labelled red cell scan
C	Isotope-labelled white cell scan
D	Tissue transglutaminase antibodies
E	Bone marrow aspirate and trephine

D Tissue transglutaminase antibodies

This gentleman’s anaemia is due to iron deficiency, and the most likely cause is blood loss within the gastrointestinal tract. Repeating invasive imaging is unlikely to have as high a yield as tissue transglutamase antibodies, which may reveal an underlying diagnosis of coeliac disease, particularly as this patient failed to tolerate the gastroscopy well last time.

B Isotope-labelled red cell scan

Isotope-labelled red cell scans are useful to exclude significant bleeding, not the limited chronic blood loss which is likely here.

A Repeat colonoscopy and gastroscopy

An adequately prepared colonoscopy and gastroscopy is likely to exclude

An adequately prepared colonoscopy and gastroscopy is likely to exclude significant pathology from the oesophagus, stomach and colon, and thus repeating them has limited utility versus other investigations.

C	Isotope-labelled white cell scan

Isotope-labelled white cell scans are most useful in locating occult intra-abdominal abscesses.

E	Bone marrow aspirate and trephine

Given that there is evidence of iron deficiency anaemia, bone marrow examination is not of value in this case.

6388

Question 15 of 42

An 18-year-old woman presents with an episode of epistaxis, which settles with conservative management. Apparently she has had a recent flu-like illness.

On examination, she has a number of petechiae and some bruising where she has taken knocks or bangs to her legs. She is on no significant medication and has a clean past medical history. You understand that her aunt had a splenectomy as a young adult.

Investigations:

Hb	11.0 g/dl
WCC	5.0 x10^9/l
PLT	16.0 × 10^9/l
Na$^+$	139 mmol/l
K$^+$	4.0 mmol/l
Creatinine	105 µmol/l

Which of the following is the most appropriate treatment?

WCC	5.0 x10⁹/l
PLT	16.0 × 10⁹/l
Na⁺	139 mmol/l
K⁺	4.0 mmol/l
Creatinine	105 µmol/l

Which of the following is the most appropriate treatment?

A	Platelet transfusion
B	Prednisolone 20 mg daily
C	Prednisolone 60 mg daily
D	Splenectomy
E	Azathioprine 100 mg daily

20556

Question 15 of 42

On examination, she has a number of petechiae and some bruising where she has taken knocks or bangs to her legs. She is on no significant medication and has a clean past medical history. You understand that her aunt had a splenectomy as a young adult.

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PLT	16.0 × 10^9/l
Na^+	139 mmol/l
K^+	4.0 mmol/l
Creatinine	105 µmol/l

Which of the following is the most appropriate treatment?

Your answer was correct

A	Platelet transfusion

Question 15 of 42

C	Prednisolone 60 mg daily

This patient has idiopathic thrombocytopaenic purpura (ITP). Over recent years a familial propensity for the development of ITP has been identified, although the particular gene for susceptibility is yet to be identified. First-line treatment involves the use of high-dose corticosteroids with or without IV immunoglobulins. Thrombopoietin receptor agonists may also reduce the need over the longer term for splenectomy.

A	Platelet transfusion

Platelet transfusions may be required for uncontrolled haemorrhage, although they don’t reduce the underlying autoantibody burden resulting in platelet destruction. They are not therefore the initial intervention of choice.

B	Prednisolone 20 mg daily

Question 15 of 42

resulting in platelet destruction. They are not therefore the initial intervention of choice.

B	Prednisolone 20 mg daily

This dose is likely to prove inadequate to reduce immune-mediated platelet destruction significantly.

D	Splenectomy

Splenectomy is required for patients who don’t respond to immune intervention for treatment of their thrombocytopenia.

E	Azathioprine 100 mg daily

Azathioprine is a potential steroid-sparing agent in the treatment of ITP in patients who are unable to significantly reduce their dose of prednisolone without a fall in platelet count.

20556

Rate this question: ☆☆☆☆☆

You are asked to the Accident and Emergency Department (A&E) to see middle-aged gentleman who has been found unconscious. He has been brought in by ambulance and there is no medical history available, although he has apparently attended A&E in an intoxicated state on a number of occasions over the past year. He has a packet of vitamin tablets but no identifying information.

On examination, his temperature is 36.3 °C, blood pressure 105/65 mmHg and pulse 98 beats per minute. He has a Glasgow coma scale of 9/15 and is breathing deeply. Cranial nerves are intact and peripheral reflexes are normal. A spleen tip is palpable. He has palmar erythema, is jaundiced and has several spider naevi over his chest. Rectal examination reveals melaena.

Investigations:

Hb	98 g/dl
WCC	2.5 x 10^9/l
PLT	102 × 10^9/l

Question 16 of 42

Hb	98 g/dl
WCC	2.5 x 10^9/l
PLT	102 × 10^9/l
Fibrinogen	0.5g/l (1.8–5.4)
APTT	42 s (30–40 s)
PT	17 s (11.5–15.5 s)

What is the most appropriate blood product to use in this situation?

A	Two units of packed red cells
B	15ml/kg of fresh frozen plasma
C	IV Factor VIII
D	Platelet transfusion
E	10 mg IV vitamin K

Question 16 of 42

Hb	98 g/dl
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A	Two units of packed red cells
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D	Platelet transfusion

Question 16 of 42

B 15ml/kg of fresh frozen plasma

This gentleman has advanced liver disease with portal hypertension and hypersplenism. He is bleeding internally - possibly from varices, a common cause of hepatic encephalopathy - and has deranged clotting, the most notable feature of which is the low fibrinogen. This is best replaced with cryoprecipitate, which is rich in factor VIII and fibrinogen, although current NICE guidance does not assume widespread availability of cryoprecipitate and therefore recommends FFP, which contains a smaller amount of fibrinogen.

A Two units of packed red cells

Although there may be a fall in Hb once adequate fluid resuscitation is initiated, replacing packed cells won't reduce the risk of further bleeding.

C IV Factor VIII

Question 16 of 42

C IV Factor VIII

Factor VIII replacement alone won’t adequately reduce bleeding tendency; a source of fibrinogen is also required, which is why cryoprecipitate is preferred.

D Platelet transfusion

Platelet transfusion is of little value where platelets are above 50, and is only usually considered when platelets are below 20 in the face of active bleeding.

E 10 mg IV vitamin K

The PT is not significantly prolonged, and vitamin K will therefore have very limited impact in reducing the risk of further bleeding.

6389

Rate this question: ☆☆☆☆☆

Question 17 of 42

A 45-year-old woman is referred for investigation of a paraprotein found at a Well-Woman check. She is currently asymptomatic and working full-time as a teacher. She is on no medication and does not smoke. She has three sisters who are all well.

On examination, pulse is 90 beats per minute, blood pressure 110/64 mmHg, heart sounds normal, chest is clear. There is no palpable lymphadenopathy or organomegaly. Neurological examination is unremarkable, with normal fundoscopy and intact sensation.

Investigations:

Hb	14.3 g/dl
WCC	6.3 x 10^9/l
Platelets	355 x 10^9/l
Na^+	138 mmol/l
K^+	4.5 mmol/l
Creatinine	100 µmol/l
Protein	

Question 17 of 42

Protein electrophoresis	M band present
Paraprotein quantification IgG kappa	12 g/l
Serum corrected calcium	2.24 mM
Urine	negative for Bence Jones protein
Skeletal survey	unremarkable
Bone marrow aspirate	shows 25% plasma cells
Karyotyping	no high risk features

What is the most appropriate management?

A Regular follow up with blood tests only

B Melphalan and prednisolone

	protein
Skeletal survey	unremarkable
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What is the most appropriate management?

A Regular follow up with blood tests only

B Melphalan and prednisolone

C Thalidomide and dexamethasone

D Bortezomib

E Vincristine, doxorubicin and dexamethasone

Question 17 of 42

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Na^+	138 mmol/l
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Bone marrow aspirate	shows 25% plasma cells
Karyotyping	no high risk features

What is the most appropriate

A Regular follow up with blood tests only

This patient has probable early myeloma – bone marrow diagnostic of myeloma, but IgG paraprotein of less than 30 g/l and with no evidence of myeloma-associated organ damage (i.e. normal blood count, calcium, renal function and skeletal survey). In this case, early treatment has so far not been proven to change the course of the illness.

B Melphalan and prednisolone

Melphalan is reserved for the treatment of myeloma in more elderly patients with co-morbidities for whom more aggressive intervention is inappropriate.

C Thalidomide and dexamethasone

Thalidomide is a component of modern

Question 17 of 42

C	Thalidomide and dexamethasone

Thalidomide is a component of modern myeloma therapy regimens, and is thought to be effective because of anti-angiogenic properties. It is used in triple combination with dexamethasone and bortezomib.

D	Bortezomib

Bortezomib inhibits the 26S proteasome and is therefore an indirect inhibitor of nuclear factor kappa B, leading to apoptosis. It is used as an induction chemotherapy agent in some regimens.

E	Vincristine, doxorubicin and dexamethasone

This was previously considered the gold standard protocol for myeloma, although this has now been largely superseded by better-tolerated, more effective combination regimens.

Question 18 of 42

A 28-year-old man is newly diagnosed with acute myeloid leukaemia (AML). He receives an initial dose of chemotherapy on day 1 and has become neutropenic at day 7.

At day 14, he is given a broad-spectrum antibiotic after admission via the Emergency Department for fever and rigors. His indwelling catheter is not infected, but unfortunately the fever does not respond. At day 16 there is a cavitating lesion on his chest X-ray.

Which of the following represents the most likely diagnosis?

A	Tuberculosis
B	Invasive *Aspergillus fumigatus*
C	Cytomegalovirus
D	Coagulase-negative *Staphylococcus*

Question 18 of 42

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B Invasive *Aspergillus fumigatus*

C Cytomegalovirus

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E *Pneumocystis jirovecii* pneumonia (PCP)

6630

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Which of the following represents the most likely diagnosis?

Your answer was incorrect

A	Tuberculosis
B	Invasive *Aspergillus fumigatus*
C	Cytomegalovirus

B Invasive *Aspergillus fumigatus*

The acute onset of fever and rigors in a neutropenic patient and the failure to respond to antibiotics, coupled with the lesion on chest X-ray, suggest infection with *Aspergillus*. The most common infections in the neutropenic patient are Gram-positive bacterial infections (60%), such as *Staphylococcus epidermidis*. Gram-negative infections, such as *Escherichia coli*, also occur with relatively high frequency (30%). Fungal infections occur in less than 10% of patients, but are more likely in those with profound and prolonged neutropenia and pre-existing lung disease.

E *Pneumocystis jirovecii* pneumonia (PCP)

PCP may be seen in patients with neutropenia although patchy alveolar infiltration, rather than cavitation, is the more usual finding.

Question 18 of 42

A Tuberculosis

Primary tuberculosis lesions are not usually associated with cavitation, with caseating granuloma formation including calcification much more usual.

C Cytomegalovirus

Patchy infiltration is usually seen on the CXR in patients suffering from CMV pneumonitis, rather than the discrete area of calcification seen here.

D Coagulase-negative *Staphylococcus*

Coagulase negative *Staphylococcus* would usually be covered by the broad-spectrum antibiotic approach taken in the treatment of patients with febrile neutropenia.

6630

Rate this question: ☆☆☆☆☆

Question 19 of 42

A 28-year-old woman comes to the Haematology Clinic for review. She has developed a right calf DVT without any precipitating risk factors.

Her only medication of note was the oral contraceptive pill, which she has now stopped and is making alternative arrangements for contraception. She is screened for thrombophilia and is found to be heterozygous for factor V Leiden deficiency.

For how long should she be warfarinised?

A 1 month

B 3 months

C 6 months

D 1 year

E Lifelong

Question 19 of 42

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Her only medication of note was the oral contraceptive pill, which she has now stopped and is making alternative arrangements for contraception. She is screened for thrombophilia and is found to be heterozygous for factor V Leiden deficiency.

For how long should she be warfarinised?

Your answer was correct

A 1 month

B 3 months

C 6 months

D 1 year

Question 19 of 42

C 6 months

Without pre-disposing risk factors, guidelines suggest that anticoagulation is continued for 3–6 months in total. Given that we know that this patient is heterozygous for factor V Leiden, it would seem sensible to continue the warfarin for 6 months. Recent population analyses/case series have, however, now suggested that the risk–benefit for lifelong warfarin in a patient with factor V Leiden who has a first DVT may not be positive, due to bleeding risk. As such, lifelong warfarin is no longer recommended in this situation for a first event.

A 1 month

Most patients with a first episode of venous thromboembolism (VTE; provoked or unprovoked) should receive anticoagulation for a minimum of 3 months. Extending anticoagulation beyond 3 months is not routinely considered in patients who have a

Question 19 of 42

considered in patients who have a provoked episode of VTE with the following: transient risk factors, assuming the risk factor is no longer present (e.g. surgery, cessation of hormonal therapy), isolated distal DVT, sub-segmental or incidental pulmonary embolism (PE) or those in whom the risk of bleeding is considered to be high.

B 3 months

This lady has no predisposing factors, so 3–6 months is the recommended duration for anticoagulation. Given that she is heterozygous for factor V Leiden deficiency, it would be sensible to continue up to 6 months.

D 1 year

The benefits of prolonged anticoagulation (6–12 months) even in selected populations (e.g. persisting but reversible risk factor) are unproven.

B	3 months

This lady has no predisposing factors, so 3–6 months is the recommended duration for anticoagulation. Given that she is heterozygous for factor V Leiden deficiency, it would be sensible to continue up to 6 months.

D	1 year

The benefits of prolonged anticoagulation (6–12 months) even in selected populations (e.g. persisting but reversible risk factor) are unproven.

E	Lifelong

There is no benefit in lifelong anticoagulation in patients with factor V Leiden deficiency.

34962

Question 1 of 23

A 37-year-old woman is admitted with confusion. She has no past medical history of note and was previously fit and well.

Examination reveals small petechial haemorrhages on the legs and pale conjunctivae. Her abdomen is soft and non-tender, with no organomegaly detectable. Chest is clear and thorough systemic examination reveals no abnormalities except for a fluctuant Glasgow Coma Scale.

Observations: heart rate 110 bpm, BP 115/72 mmHg, temperature 38.4 °C and O_2 sats 97% on room air.

Investigations:

Hb	9.3 g/dl !120–155)
WCC	13 × 10^9/l (4.0–11.0)
PLT	34 × 10^9/l (150–450)
Na^+	142 mmol/l (135–145)
K^+	5.1 mmol/l (3.5–5.3)

Creatinine	168 µmol/l (45–84)
Plasma haptoglobulin	0.19 g/l (0.3–2.0)
Urea	11.2 mmol/l (2.5–7.8)
CRP	8 mg/l (<5)
Bilirubin	35 µmol/l (3–17)
ALT	38 IU/l (<40)
ALP	100 IU/l (40–130)
GGT	32 IU/l (10–50)
Albumin	38 g/l (35–50)
Urine dipstick	Blood+, protein+
Blood film	Schistocytes
Chest X-ray	Lung fields clear, no other abnormalities detected

Question 1 of 23

Blood film	Schistocytes
Chest X-ray	Lung fields clear, no other abnormalities detected

What is the most likely diagnosis?

A	Henoch–Schönlein purpura (HSP)
B	Thrombotic thrombocytopenic purpura (TTP)
C	Haemolysis, elevated liver enzymes and low platelet count (HELLP) syndrome
D	Chest sepsis
E	Systemic lupus erythematosus (SLE)

7073

B Thrombotic thrombocytopenic purpura (TTP)

TTP is classically associated with the pentad of clinical signs and findings: confusion, pyrexia, kidney disease, thrombocytopenia and microangiopathic haemolytic anaemia. The patient in this case exhibits all of these criteria, although it should be noted that not all patients will display all five.

Thrombotic thrombocytopenic purpura is a condition that causes a microangiopathic haemolytic anaemia. The exact aetiology is unclear, but it has been found to be associated with auto-antibodies to ADAMTS13, a protein responsible for cleaving von Willebrand factor (VWF) into smaller units. Ultra-long VWF is very pro-thrombotic and can form a mesh in the vessels which causes fragmentation of red cells (a microangiopathic haemolytic anaemia). It can be associated with pregnancy and the

haemolytic anaemia). It can be associated with pregnancy and the postpartum period, but is also seen in non-pregnant individuals. TTP is characterised by five symptoms or signs: confusion, pyrexia, kidney disease, thrombocytopenia and microangiopathic haemolytic anaemia. Patients are often treated with plasma exchange. Eculizumab may be useful in patients with refractory disease.

A	Henoch–Schönlein purpura (HSP)

HSP classically affects children post-mild infection. This would be a differential diagnosis for petechial haemorrhages on the patient’s legs, but this patient is suffering from many other symptoms (fever and confusion) which would not be explained by HSP. Furthermore, whilst HSP can cause deranged renal function, the low platelet count, raised bilirubin and signs of haemolysis on the blood film seen in this case are not associated with HSP.

C Haemolysis, elevated liver enzymes and low platelet count (HELLP) syndrome

HELLP syndrome is associated with confusion, haemolysis and low platelets, as seen in this case. However, it is only seen in the setting of pregnancy, or recent delivery, usually associated with pre-eclampsia.

D Chest sepsis

Sepsis can present very similarly to TTP, i.e. with a fever, confusion and signs of microangiopathic haemolytic anaemia (if deteriorated to disseminated intravascular coagulation) and is always a very important differential diagnosis to be considered in these patients. However, the history and examination suggest that there is no clear source of sepsis, the patient’s CRP is not raised and the chest X-ray is normal.

E Systemic lupus

considered in these patients. However, the history and examination suggest that there is no clear source of sepsis, the patient's CRP is not raised and the chest X-ray is normal.

E	Systemic lupus erythematosus (SLE)

SLE is the great mimic and can affect all organs including the kidneys, brain and blood. However, SLE is a more chronic condition than the history described here. Furthermore, if this answer referred to SLE flares, these are typically in the context of a history of SLE, which this patient does not have and commonly presents with painful joints, rashes and fatigue. Therefore, this is not the most likely diagnosis.

7073

Question 2 of 23

A 53-year-old gentleman was admitted with right-sided hemiparesis. He was known to be on warfarin for a mitral valve replacement and had been adequately anticoagulated. He was taking furosemide and had recently started taking St John's wort for low mood.

On examination, his pulse was 90 beats/min and regular, and his blood pressure was 150/80 mmHg. Cardiac examination demonstrated normal prosthetic valve sounds with an ejection systolic murmur at the left sternal edge. The patient had a right-sided hemiparesis and right upper motor neuron VII nerve palsy.

A computed tomography (CT) scan shows evidence of a left middle cerebral artery infarction.

What is a possible explanation for the presentation?

A	St John's wort is prothrombotic

A computed tomography (CT) scan shows evidence of a left middle cerebral artery infarction.

What is a possible explanation for the presentation?

A	St John's wort is prothrombotic
B	St John's wort reduces the activity of warfarin
C	St John's wort increases platelet aggregation
D	St John's wort increases blood cholesterol levels
E	St John's wort causes vasospasm of the cerebral vessels

33312

Question 2 of 23

B St John's wort reduces the activity of warfarin

St John's wort reduces the INR because it is a potent inducer of cytochrome P450, thus leading to greatly increased warfarin metabolism. Careful monitoring of INR is therefore required if a patient on warfarin wishes to take St John's wort, with up-titration of the warfarin dose according to INR. Ideally an alternative antidepressant should be considered if required, and they should be warned if they do take it that dose reduction of warfarin will be needed when they discontinue the herbal remedy. Echocardiography should also be considered to exclude valve thrombosis, but the immediate priority is assessing and correcting his coagulation status.

A St John's wort is prothrombotic

It is a liver enzyme inducer.

Question 2 of 23

C St John's wort increases platelet aggregation

It is a liver enzyme inducer, thus increasing the metabolism of warfarin and decreasing the INR, subsequently predisposing to embolic/thrombotic episodes.

D St John's wort increases blood cholesterol levels

It is a liver enzyme inducer affecting the metabolism of warfarin.

E St John's wort causes vasospasm of the cerebral vessels

Cerebral vasospasm can be a complication of subarachnoid haemorrhage. The traditional treatment of subarachnoid haemorrhage (SAH) from a ruptured cerebral aneurysm included strict blood pressure control, with fluid restriction and antihypertensive

A 40-year-old female patient on the Haematology Ward has become increasingly unwell over the past few days. She is 2 weeks' post-allogenic haemopoietic stem cell transplant (HSCT) for acute myeloid leukaemia.

On examination, she is jaundiced with ascites, hepatomegaly and right upper quadrant tenderness. Further examination reveals bi-basal inspiratory crepitations and peripheral oedema.

Initial investigations:

Hb	8.9 g/dl (120–155)
WCC	2.8 × 10^9/l (4.0–11.0)
Neutrophil count	1.8 × 10^9/l (2.0–7.5)
PLT	60 × 10^9/l (150–450)
Bilirubin	119 µmol/l (3–17)
ALT	39 IU/l (<40)
ALP	290 IU/l (40–130)
GGT	260 IU/l (10–50)

Question 3 of 23

Albumin	28 g/l (35–50)
CRP	9 mg/l (<5)
Portable chest X-ray	Upper lobe diversion with blunted right costophrenic angle
Pre and post-transplant viral screens	-

What is the most likely diagnosis?

A	Veno-occlusive disease of the liver
B	Hepatitis B infection
C	Transfusion-associated cardiac overload (TACO)
D	Cyclosporin toxicity
E	Cholangitis

Question 3 of 23

days. She is 2 weeks’ post-allogenic haemopoietic stem cell transplant (HSCT) for acute myeloid leukaemia.

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GGT	260 IU/l (10–50)
Albumin	28 g/l (35–50)
CRP	9 mg/l (<5)

Question 3 of 23

A Veno-occlusive disease of the liver

This patient is exhibiting signs and investigation findings suggestive of veno-occlusive disease of the liver. Veno-occlusive disease of the liver, otherwise known as sinusoidal obstruction syndrome, is a serious complication of allogeneic stem cell transplantation that can rarely occur within 2 weeks of the transplant. The pathophysiology is unclear, but is thought to be related to the patient's inherent haemostatic derangements.

Classically the patient will start to gain weight, become oedematous, jaundiced and have ascites with tender hepatomegaly. Blood tests will show a hyperbilirubinaemia with often a raised ALP and GGT. A Doppler ultrasound scan will help in confirming the diagnosis, and histology would reveal centrilobular necrosis. Management is difficult and includes maintaining fluid volume while treating ascites and pulmonary oedema. Other treatments tried include heparin and tissue

tried include heparin and tissue plasminogen activator. These patients are at risk of developing multi-organ failure and are often best managed on the intensive therapy unit (ITU) with the transplant team's daily input.

Of note, two weeks' post-transplant, the patient's haemoglobin, platelet, white cell counts and white cell differentials will still be low, although hopefully climbing, as the donor stem cells engraft in the patient's bone marrow and start to produce normal blood cell precursors. This patient's full blood count is therefore not unusual in these circumstances. Post-stem cell transplant patients are only transfused blood products if (1) their Hb is <8.0 g/dl; (2) their platelet count is <10 × 10^9/l or <20 × 10^9/l and septic, or the patient is bleeding; or (3) their platelet count is too low to safely have a necessary procedure.

D Cyclosporin toxicity

Ciclosporin (used post-HSCT to prevent graft-vs-host disease) is a

prevent graft-vs-host disease) is a toxic medication and requires close drug level monitoring. It classically causes gastrointestinal side effects including diarrhoea and nausea, skin side effects including rashes and can be nephrotoxic. Ciclosporin toxicity is not associated with acute fluid overload as seen in this case.

B	Hepatitis B infection

Hepatitis B would be unlikely to present acutely with fluid overload. Furthermore, all patients receiving HSCT (as for solid tumour transplants) are required to have a full viral screen prior to transplant, including HIV, hepatitis B and C, CMV and EBV. This patient's viral screens were negative.

C	Transfusion-associated cardiac overload (TACO)

Patients post-HSCT are very susceptible to TACO, as they receive a very large number of blood products. However, this patient is exhibiting

are required to have a full viral screen prior to transplant, including HIV, hepatitis B and C, CMV and EBV. This patient's viral screens were negative.

C	Transfusion-associated cardiac overload (TACO)

Patients post-HSCT are very susceptible to TACO, as they receive a very large number of blood products. However, this patient is exhibiting upper right quadrant pain and her liver function is markedly deranged, pointing away from TACO.

E	Cholangitis

This patient's CRP is unremarkable, which points away from acute inflammation. However, post-transplant patients are very susceptible to infection and this would be a fair differential diagnosis.

Question 1 of 20

A 67-year-old woman is reviewed on the ITU after having presented with hypotension, tachycardia and pyrexia. She has been intubated and ventilated, and treatment with IV co-amoxiclav commenced.

Forty-eight hours later, she is deteriorating, requiring noradrenaline support and her creatinine has increased from 145 µmol/l on admission to 235 µmol/l. CRP and white count remain elevated at 310 mg/l and 15.2 x10^9/l, respectively. Glucose is 8.1 mmol/l.

Which of the following is the most appropriate next step?

A	Add hydrocortisone to the regimen
B	Change the antibiotic regime to vancomycin and piperacillin/tazobactam
C	Institute intensive insulin therapy

Question 1 of 20

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Which of the following is the most appropriate next step?

A	Add hydrocortisone to the regimen
B	Change the antibiotic regime to vancomycin and piperacillin/tazobactam
C	Institute intensive insulin therapy
D	Increase the dose of noradrenaline
E	Start additional dopamine therapy

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Question 1 of 20

B	Change the antibiotic regime to vancomycin and piperacillin/tazobactam

This woman has signs of ongoing sepsis, as evidenced by her raised inflammatory markers and ongoing hypotension requiring noradrenaline support, and it is likely that the co-amoxiclav has provided inadequate coverage so far. As such, switching to a combination with wide coverage and activity versus *Pseudomonas* is most appropriate, such as vancomycin and piperacillin/tazobactam.

A	Add hydrocortisone to the regimen

Guidelines recommend against the routine use of glucocorticoids in patients with sepsis. Hydrocortisone may have a role in the presence of severe sepsis not responding to adequate fluid resuscitation and vasopressors.

C Institute intensive insulin therapy

Capillary blood glucose should be monitored carefully and IV insulin infusion should be started if capillary blood glucose is persistently higher than 12 mmol/l and the patient is unable to eat and drink. For people with type 1 diabetes, the long-acting insulin should be continued at all times. In our case, capillary blood glucose of 8.1 mmol/l doesn’t require intervention.

Concern about the potentially deleterious effects of hyperglycaemia in critically ill patients has motivated multiple randomized controlled trials investigating glycaemic management in ICUs. Several subsequent studies conducted in a variety of settings similarly failed to demonstrate clear benefits to tight glycaemic control in critically ill patients, but consistently highlighted an increased risk of hypoglycaemia among patients treated with intensive insulin protocols.

hypoglycaemia among patients treated with intensive insulin protocols.

D	Increase the dose of noradrenaline

In the present case, there is still the option to escalate the antibiotic therapy prior to increasing the dose of noradrenaline.

E	Start additional dopamine therapy

In patients who remain hypotensive despite adequate fluid resuscitation, appropriate antibiotic choice and noradrenaline, the addition of a second or third agent to noradrenaline may be required (e.g. adrenaline, dobutamine or vasopressin) with little data to support agent selection. Some studies showed improved survival with dobutamine. In the present case, there is still room for antibiotic escalation prior to the addition of a second inotropic agent.

A 22-year-old student is brought to the Emergency Department with recurrent seizures. He had collapsed at the bar and had witnessed seizures. His flatmate reckoned he had nine cocktails that evening. Over the last few weeks he had been missing his first morning lecture and complained of intermittent fever and a dry cough. Intravenous lorazepam terminated the seizure.

On examination, he is lethargic and pale with bruises over his left arm, leg and his right buttock. His temperature is 37.8 °C, pulse 104 bpm and regular, BP 120/68 mmHg. He has gum hypertrophy, poor dentition but no mouth ulcers. His liver had descended to 2 cm but the spleen is not palpable. Neurological examination is symmetrical. Fundoscopy is unremarkable.

Investigations:

U&E	Normal
Ca^{2+}	2.43 mmol/l

5:08

Question 2 of 20

U&E	Normal
Ca^{2+}	2.43 mmol/l
Bilirubin	12 µmol/l
ALT	108 U/l
ALP	51 U/l
Glucose	5.2 mmol/l
Albumin	35 g/l
GGT	101 U/l
CRP	62 mg/l
WCC	105.2×10^9/l
Hb	7.3 g/dl
PLT	65×10^9/l
MCV	101 fl

You call the haematology registrar, who immediately performs a bone marrow biopsy which shows the presence of multiple blasts and Auer rods.

Bone marrow cytochemistry:

rods.

Bone marrow cytochemistry:

Sudan Black	+
Myeloperoxidase	+
Periodic acid–Schiff	-
Non-specific esterase	++

What is the diagnosis?

A	Acute lymphoblastic leukaemia
B	Bacterial meningitis
C	Promyelocytic leukaemia
D	Acute monocytic leukaemia
E	Human T-cell lymphoma virus type-I

Question 2 of 20

Glucose	5.2 mmol/l
Albumin	35 g/l
GGT	101 U/l
CRP	62 mg/l
WCC	105.2 × 10^9/l
Hb	7.3 g/dl
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Bone marrow cytochemistry:

Sudan Black	+
Myeloperoxidase	+
Periodic acid–Schiff	-
Non-specific esterase	++

What is the diagnosis?

Question 2 of 20

D Acute monocytic leukaemia

This patient presents with a short history of increasing malaise followed by a grand mal seizure. High counts of circulating blasts (>100 × 10^9/l) may lead to symptoms of cellular hyperviscosity (headache, confusion, fits, focal neurology and coma). Tissue deposits of leukaemic cells (e.g. causing gum hypertrophy) are common in the myelomonocytic and monocytic varieties of acute monocytic leukaemia. Auer rods are a typical finding on bone marrow biopsies. Acute monocytic leukaemia cells characteristically stain positive for Sudan black and myeloperoxidase.

C Promyelocytic leukaemia

This is a subtype of acute myeloid leukaemia (AML). Patients can present with pallor, non-specific infections, thrombocytopenia, petechiae, hepatomegaly, splenomegaly and gingivitis. Cytogenetic studies are

hepatomegaly, splenomegaly and gingivitis. Cytogenetic studies are useful in identifying patients with promyelocytic leukaemia as they will have translocation of the long-arm chromosomes of 15 and 17. There will also be Auer rods present on blood films.

A	Acute lymphoblastic leukaemia

Patients usually present with recurrent infections, bone and joint pain, fatigue, splenomegaly, headaches or complications due to DIC. Patients usually have a raised white cell count, raised LDH and severe anaemia. Blood films show blast cells. For a diagnosis of ALL, there needs to be over 20% blast cells on bone marrow biopsy. Treatment usually consists of short-term intensive chemotherapy initially for remission induction followed by consolidation and maintenance.

B	Bacterial meningitis

consolidation and maintenance.

B	Bacterial meningitis

Bacterial meningitis is a reasonable consideration in a student who presents with a history of fevers and seizures. However, the other symptoms such as gum hypertrophy and bruising, coupled with his investigation findings, do not fit with a diagnosis of bacterial meningitis.

E	Human T-cell lymphoma virus type-I

This virus is known to cause a highly aggressive non-Hodgkin's lymphoma. It often causes hypercalcaemia, visceral involvement, skin lesions and lytic bone lesions. This is not in keeping with the patient in this case. meaning that this is unlikely to be the diagnosis.

A 65-year-old lady attends the Emergency Department complaining of increasing lower back pain, after a weekend of gardening. Her symptoms are relieved with ibuprofen. She denies any bowel or bladder symptoms, and is able to weight bear. She has a past medical history of osteoarthritis of the neck, type 2 diabetes and carcinoma of the colon, which was treated by hemicolectomy 3 years previously.

On examination, heart sounds are normal, the chest is clear, there is a laparotomy scar but no organomegaly and anal tone is normal. Cranial and peripheral nervous system examination are normal.

Investigations:

Hb	10.2 g/dl
WCC	$5.1 \times 10^9/l$
Neutrophils	$2.5 \times 10^9/l$
Lymphocytes	$2.0 \times 10^9/l$
Monocytes	$0.5 \times 10^9/l$
Eosinophils	$0.1 \times 10^9/l$

Eosinophils	0.1 × 10^9/l
Basophils	0.01 × 10^9/l
MCV	82 fl
MCH	27 pg
MCHC	5 x 10^9/l
PLT	250 × 109/l
Sodium	138 mmol/l
Potassium	4.5 mmol/l
Urea	7.4 mmol/l
Creatinine	130 µmol/l
Bilirubin	10 µmol/l
Albumin	32 g/l (37–49)
ALP	55 U/l (45–105)
AST	20 U/l (1–31)
Protein	85 g/l (61–76)
Calcium	2.5 mmol/l (2.2–2.6)
Phosphate	0.9 mmol/l (0.8–1.4)

Calcium	2.5 mmol/l (2.2–2.6)
Phosphate	0.9 mmol/l (0.8–1.4)

Which one of the following tests would best confirm the suspected underlying diagnosis?

A	Bone scan
B	Serum tumour markers
C	Blood film
D	Bone marrow aspirate
E	Urine dipstick for protein

33303

Question 3 of 20

Basophils	0.01 × 10^9/l
MCV	82 fl
MCH	27 pg
MCHC	5 x 10^9/l
PLT	250 × 109/l
Sodium	138 mmol/l
Potassium	4.5 mmol/l
Urea	7.4 mmol/l
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Protein	85 g/l (61–76)
Calcium	2.5 mmol/l (2.2–2.6)
Phosphate	0.9 mmol/l (0.8–1.4)

Which one of the following tests

D Bone marrow aspirate

The patient has myeloma, as suggested by the history of bone pain and the findings of a normocytic anaemia, mild renal impairment and a raised total protein in the presence of an albumin just below the normal range, indicating the presence of raised immunoglobulins.
Myeloma is a clonal B-cell malignancy characterised by proliferation of plasma cells that accumulate mainly in bone marrow and usually secrete paraprotein. It accounts for 1% of all malignancies and 10% of haematological malignancies. Bone marrow plasma cell load is a key criterion for the diagnosis of myeloma and, as such, is the correct answer here.

Diagnostic criteria for myeloma: International myeloma working group 2015:

Clonal bone marrow plasma cells >10% or biopsy-proven bony or extramedullary plasmacytoma and any

Question 3 of 20

or biopsy-proven bony or extramedullary plasmacytoma and any one or more of the following features and myeloma-defining events:

- Evidence of end organ damage that can be attributed to the underlying plasma cell proliferative disorder, specifically:
  - Hypercalcaemia: serum calcium >0.25 mmol/l higher than the upper limit of normal or >2.75 mmol/l
  - Renal insufficiency: creatinine clearance <40 ml per minute or serum creatinine >177 mmol/l
  - Anaemia: haemoglobin value of >20 g/l below the lowest limit of normal, or a haemoglobin value <100 g/l
  - Bone lesions: one or more osteolytic lesion on skeletal radiography, CT or PET/CT. If bone marrow has <10% clonal plasma cells, more than one bone lesion is

- Bone lesions: one or more osteolytic lesion on skeletal radiography, CT or PET/CT. If bone marrow has <10% clonal plasma cells, more than one bone lesion is required to distinguish from solitary plasmacytoma with minimal marrow involvement.

- Any one or more of the following biomarkers of malignancy:
  - 60% or greater clonal plasma cells on bone marrow examination
  - Serum involved/uninvolved free light chain ratio of 100 or greater, provided the absolute level of the involved light chain is at least 100 mg/l
  - More than one focal lesion on MRI that is at least 5 mm or greater in size.

A	Bone scan

Question 4 of 20

A 29-year-old man presents to the Emergency Department. He has suffered from nearly three hours of severe central chest pain. ECG shows clear evidence of an anterior myocardial infarction.

Other past medical history of note includes severe short-sightedness; he has also suffered from joint laxity with recurrent shoulder dislocation and a left inguinal hernia.

On examination, he is slim, with a BMI of 21, and is 190 cm in height.

Investigations:

Hb	12.1 g/dl
WCC	4.8 × 10^9/l
PLT	210 × 10^9/l
Na^+	132 mmol/l
K^+	5.1 mmol/l
Creatinine	120 µmol/l
Urea	5.4 mmol/l
Total cholesterol	5.1 mmol/l

Question 4 of 20

K⁺	5.1 mmol/l
Creatinine	120 µmol/l
Urea	5.4 mmol/l
Total cholesterol	5.1 mmol/l

Which of the following diagnoses fits best with the underlying cause of his myocardial infarction?

A	Protein C deficiency
B	Protein S deficiency
C	Familial mixed hyperlipidaemia
D	Homocystinuria
E	Cystinuria

18522

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Urea	5.4 mmol/l

D Homocystinuria

This man has a history of short-sightedness, ligamentous laxity and thromboembolic phenomena, all of which fit with the possibility of homocystinuria. Marfan syndrome would be associated with ligamentous laxity and lens dislocation, but also with aortic dissection rather than thromboembolic phenomena. Psychiatric features may be seen in up to 50% of patients with homocystinuria, and pyramidal tract symptoms may also be seen. The skin is usually pale and pink, and occasionally livedo reticularis and a malar rash may be seen. Diagnosis may be based on urinary homocysteine levels or other parameters, such as measuring cystathione synthase activity in liver biopsy samples. Possible treatments include pyridoxine and folic acid.

A Protein C deficiency

Protein C deficiency is associated with

Protein C deficiency is associated with increased risk of venous thromboembolism, but not with the marfanoid features seen here.

B	Protein S deficiency

Like protein C deficiency, protein S deficiency can lead to increased risk of venous thromboembolism, although it isn’t associated with marfanoid features.

C	Familial mixed hyperlipidaemia

Familial mixed hyperlipidaemia is unlikely given that his total cholesterol is 5.1 mmol/l. High-dose statin therapy is the intervention of choice where there is marked hypercholesterolaemia.

E	Cystinuria

Cystinuria is associated with renal stones, but not the marfanoid picture seen here or with increased risk of

Question 5 of 20

You review a woman who is 34 weeks pregnant. Fetal growth has been normal so far. She presents with epigastric pain and increasing ankle oedema.

Her midwife has noted her blood pressure to be 159/95 mmHg (increased from 132/81 mmHg some 2 weeks earlier). She has proteinuria. Platelet count is reduced at 7 × 10^9/l (down from 160 × 10^9/l some 4 weeks earlier). She has raised transaminases and bilirubin.

What would be the most appropriate treatment for this patient?

A Hydralazine IV and admit for bed rest

B Delivery of the baby post replacement of blood products

C Observation

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What would be the most appropriate treatment for this patient?

A Hydralazine IV and admit for bed rest

B Delivery of the baby post replacement of blood products

C Observation

D Oral nifedipine and discharge

E Urgent ultrasound scan of the liver

5:26

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B Delivery of the baby post replacement of blood products

This woman has evidence of pre-eclampsia, with a deteriorating blood picture (decreased platelet count and abnormal liver enzymes) and rapidly worsening hypertension. Nearly 10% of women with severe pre-eclampsia and 30–50% of women with eclampsia are affected by the syndrome of haemolysis, elevated liver enzymes and low platelet count (HELLP). The exact relationship between HELLP syndrome and pre-eclampsia is unknown. Women with pre-eclampsia and HELLP syndrome develop hepatocellular necrosis and liver dysfunction. They also have an increased mortality rate, and one third of women with pre-eclampsia develop disseminated intravascular coagulation. The best treatment for this woman would be to deliver the baby. Mild hypertension in pregnancy has been managed with oral nifedipine or labetalol. In this case, IV hydralazine or labetalol may well be

Question 5 of 20

IV hydralazine or labetalol may well be required for blood pressure reduction/control pre-op.

A	Hydralazine IV and admit for bed rest

Women with pre-eclampsia and HELLP syndrome will be unlikely to settle with blood pressure control alone, so delivery of the baby is the best treatment.

C	Observation

Women with pre-eclampsia and HELLP syndrome need treatment, so observation is incorrect.

D	Oral nifedipine and discharge

Women with pre-eclampsia and HELLP syndrome will need more than oral nifedipine for blood pressure control. It would not be appropriate to discharge without treatment.

A 72-year-old woman presents with back pain over the past several months. Additionally, she has suffered from increasing tiredness and lack of energy for the past six months. She has hypertension which is currently controlled on two oral agents and a long history of osteoarthritis affecting her hips and her back.

On examination, she looks relatively well, has a normal blood pressure (BP) of 142/82 mmHg and there are no significant findings on physical examination.

Investigations:

Hb	11.5 g/dl
WCC	5.8 × 10^9/l
PLT	201 × 10^9/l
Na^+	139 mmol/l
K^+	5.4 mmol/l
Creatinine	130 µmol/l

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Creatinine	130 µmol/l
Bone marrow	8% plasma cells
MM-protein found on electrophoresis	22 g/l

Which of the following is the most likely diagnosis?

- A Monoclonal gammopathy of unknown significance (MGUS)
- B Multiple myeloma
- C Asymptomatic myeloma
- D Myelofibrosis
- E Myelodysplasia

21224

A Monoclonal gammopathy of unknown significance (MGUS)

According to guidelines, this patient seems likely to have MGUS. The criteria for diagnosis of MGUS include an M-protein level of <30 g/l, <10% plasma cells on bone marrow investigation and no end organ damage associated with myeloma. There should also be no evidence of amyloidosis.

B Multiple myeloma

The fact that the percentage of plasma cells in bone marrow is less than 10% effectively rules out multiple myeloma here.

C Asymptomatic myeloma

Where there is no end organ damage and more than 10% of the bone marrow contains plasma cells, or M-protein is >30 g/l, then this is deemed asymptomatic myeloma.

Where there is no end organ damage and more than 10% of the bone marrow contains plasma cells, or M-protein is >30 g/l, then this is deemed asymptomatic myeloma.

D	Myelofibrosis

Myelofibrosis is associated with anaemia, with tear-drop red cells, a leuko-erythroblastic blood picture and splenomegaly, features not seen here.

E	Myelodysplasia

Unexplained macrocytic anaemia may predate the diagnosis of myelodysplasia by months or years, and neutropenia and low platelets are also seen. Splenomegaly and lymphadenopathy are very uncommonly seen in patients with myelodysplasia.

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Question 7 of 20

A 64-year-old woman was brought into the Emergency Department with a history of increasing confusion and headaches. She was noted to have multiple bruises on her shins and arms.

On examination, she had a temperature of 38 °C. There was evidence of a petechial rash over her chest. She was tachycardic and had a blood pressure of 110/65 mmHg. There was evidence of bronchial breathing at the right base and 1-cm palpable hepatosplenomegaly.

Investigations:

Haemoglobin (Hb)	55 g/l
White cell count (WCC)	18 × 10^9/l
Platelets (PLT)	20 × 10^9/l
Sodium (Na)	135 mmol/l
Potassium (K)	4.0 mmol/l

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Potassium (K)	mmol/l
Creatinine (Cr)	100 µmol/l
Prothrombin time (PT)	24 s
Activated partial thromboplastin time (APTT)	46 s
Fibrinogen	0.6 g/l (1.5–5)
Urea	6.0 mmol/l
Glucose	10.0 mmol/l
Calcium (Ca)	2.36 mmol/l
Albumin	35 g/l

What is the recommended treatment for this condition?

A Imatinib

Glucose	mmol/l
Calcium (Ca)	2.36 mmol/l
Albumin	35 g/l

What is the recommended treatment for this condition?

A	Imatinib
B	All-trans-retinoic acid (ATRA)
C	CHOP chemotherapy: cyclophosphamide, doxorubicin, vincristine and prednisolone
D	Radiotherapy
E	Fludarabine

33311

Question 7 of 20

B All-trans-retinoic acid (ATRA)

The answer is All-trans-retinoic acid (ATRA) (Option B).

The combined presentation of a chest infection, high WCC and disseminated intravascular coagulation (DIC) is typical of acute promyelocytic leukaemia (APL). The presence of DIC is suggestive of APL. DIC is a state of disruption of normal coagulation and fibrinolysis. There is activation of intravascular coagulation, leading to fibrin deposition, which causes platelet consumption (thrombocytopenia), consumption of coagulation factors (high PT and APTT) and fibrinolysis (high D-dimer). This leads to impaired coagulation and bleeding. In addition, fibrin deposition and endothelial activation lead to microvascular thrombosis, which can result in organ failure. This patient has high PT and APTT indicating coagulation factor consumption and low fibrinogen indicating fibrinolysis. Bruising and petechiae is a clinical manifestation of

indicating fibrinolysis. Bruising and petechiae is a clinical manifestation of coagulopathy in this patient. In APL, rearrangement of RARA activates promoters of tissue factors leaking to coagulation, triggering fibrin coagulation and DIC. APL cell apoptosis may also play a role, as may primary hyperfibrinolysis as a result of other prothrombotic factors.

APL is a malignancy of the bone marrow, in which there is a deficiency of mature blood cells in the myeloid line of cells and an excess of immature cells called promyelocytes. APL is considered a type of acute myeloid leukaemia (AML) and is classified as the M3 variant in the internationally accepted French-American-British (FAB) classification. APL is due to a translocation between chromosomes 15 and 17 (t(15;17)). The break in chromosome 15 disrupts the promyelocytic leukaemia (*PML*) gene, which encodes a transcription factor. The break in chromosome 17 interrupts the retinoic acid receptor alpha (*RARα*) gene, which regulates myeloid differentiation. The translocation

differentiation. The translocation creates a *PML/RARα* fusion gene, which leads to an increased proliferation of promyelocytes.

Treatment of APL differs from that for all other forms of AML. Most APL patients are now treated with all-trans-retinoic acid (ATRA). ATRA activates the retinoid receptor RAR and causes promyelocytes to differentiate, which deters them from proliferating. ATRA can induce a complete remission in most patients with APL by stimulating the APL-blasts to mature. However, ATRA cannot eliminate the leukaemic clone. ATRA is therefore used in combination with chemotherapy, including an anthracycline drug.

A	Imatinib

Imatinib (Option A) is incorrect.

Imatinib is used for chronic myelogenous leukaemia (CML) and acute lymphocytic leukaemia (ALL) that is Philadelphia chromosome-positive (Ph⁺), and in certain types of

positive (Ph⁺), and in certain types of gastrointestinal stromal tumours (GISTs), systemic mastocytosis and myelodysplastic syndrome.

C	CHOP chemotherapy: cyclophosphamide, doxorubicin, vincristine and prednisolone

CHOP chemotherapy: cyclophosphamide, doxorubicin, vincristine and prednisolone (Option C) is incorrect.

This is used for non-Hodgkin's lymphoma.

D	Radiotherapy

Radiotherapy (Option D) is incorrect.

Radiotherapy can be used in ALL or AML in cases of central nervous system involvement.

E	Fludarabine

cyclophosphamide, doxorubicin, vincristine and prednisolone (Option C) is incorrect.

This is used for non-Hodgkin's lymphoma.

D	Radiotherapy

Radiotherapy (Option D) is incorrect.

Radiotherapy can be used in ALL or AML in cases of central nervous system involvement.

E	Fludarabine

Fludarabine (Option E) is incorrect.

Fludarabine is used in the treatment of chronic lymphocytic leukaemia, AML and some types of lymphoma.

33311

A 40-year-old man presents with the complaint of worsening back pain to his GP. The pain has been present for a couple of months and is no longer relieved with analgesia.

On further questioning, the patient reports that he feels ‘tired all the time’, and has a reduced appetite with associated weight loss which he had attributed to the analgesics that he was taking. He is otherwise well at present but, 5 years previously, had been treated successfully for stage IA Hodgkin’s lymphoma. Apart from analgesics, he is on no other medication.

Positive findings on clinical examination include axillary and inguinal lymphadenopathy, 6 cm splenomegaly and tenderness along the length of his lumbar spine.

Investigations:

Hb	8.1 g/dl
WCC	12×10^9/l
Neutrophils	8×10^9/l

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WCC	12 × 10^9/l
Neutrophils	8 × 10^9/l
Promyelocytes	Increased
PLT	96 × 10^9/l
Lumbar spine X-ray	Normal

What investigation would you perform to confirm the diagnosis?

A CT scan of the thorax and abdomen

B Deoxyglucose-labelled PET scan

C Excision biopsy of an axillary lymph node

D Splenectomy

E LDH measurement

Question 8 of 20

C Excision biopsy of an axillary lymph node

The suspicion here is of marrow infiltration secondary to a recurrence of his lymphoma. Bone marrow involvement is low at the initial presentation of patients with stages I and II of Hodgkin's disease. Marrow infiltration causes anaemia, a low white cell count and thrombocytopenia. To confirm the diagnosis, a biopsy of a gland is required.

A CT scan of the thorax and abdomen

CT scan of the thorax, abdomen and pelvis usually follows a lymph node biopsy, accompanied by bone marrow investigation.

B Deoxyglucose-labelled PET scan

PET is combined with CT for staging of Hodgkin's, rather than being the initial

pelvis usually follows a lymph node biopsy, accompanied by bone marrow investigation.

B Deoxyglucose-labelled PET scan

PET is combined with CT for staging of Hodgkin’s, rather than being the initial investigation.

D Splenectomy

Splenectomy carries significant morbidity, and given that axillary lymph nodes are significantly more accessible, biopsy of an axillary lymph node is the preferred next step.

E LDH measurement

LDH is a non-specific marker of haematological malignancy and won’t help establish the underlying diagnosis.

A 62-year-old patient on warfarin for mitral valve disease and atrial fibrillation had his INR checked and it was markedly raised at 6.9.

There was no history of bleeding. He had received a course of erythromycin over the past few days for a respiratory tract infection.

Which of the following represents the most appropriate management in this case?

Your answer was correct

A Give fresh frozen plasma (FFP)

B Give vitamin K

C Give vitamin K and FFP

D Omit warfarin for a few days and monitor INR each day

D Omit warfarin for a few days and monitor INR each day

This man has a clear indication for warfarin and would be at risk of embolic stroke if his warfarin was permanently stopped. Current guidelines state that where the INR is less than 8, warfarin can be omitted for a few days and then restarted at an appropriate dose after INR has fallen. Giving vitamin K, FFP or both may confuse dosing in the future, although guidance is to give vitamin K where there is active bleeding because this alters the benefit–risk ratio of giving warfarin in a positive way.

A Give fresh frozen plasma (FFP)

FFP is given only in cases of active bleeding.

B Give vitamin K

Vitamin K is given where there is active

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FFP is given only in cases of active bleeding.

B Give vitamin K

Vitamin K is given where there is active bleeding.

C Give vitamin K and FFP

As above, vitamin K and FFP is only indicated where there is active bleeding.

E Stop the warfarin permanently

The patient is still at risk of thromboembolism due to mitral valve disease and atrial fibrillation, and he therefore still needs anticoagulation once INR is optimised.

71095

Rate this question: ⊖ ☆☆☆☆☆

Question 10 of 20

A 35-year-old patient is 1-month post-allogeneic bone marrow transplantation, when her condition deteriorates. She has developed a maculopapular rash on the palms of her hands and the soles of her feet, and has become jaundiced. The patient has also been having bouts of vomiting and diarrhoea and, as a result, has lost weight. She is currently taking ciclosporin.

Investigations:

Sodium (Na^+)	137 mmol/l
Potassium (K^+)	3.4 mmol/l
Urea	9.2 mmol/l
Creatinine (Cr)	112 µmol/l
Bilirubin	79 µmol/l
Alkaline phosphatase (ALP)	310 iu/l

Question 10 of 20

(ALP)	310 iu/l
Alanine aminotransferase (ALT)	55 iu/l
Albumin	27 g/l

Skin biopsy shows a lymphocytic infiltrate in the dermis. She is commenced on total parenteral nutrition (TPN).

Which of the following is the next best management step?

A Stop ciclosporin

B Commence methylprednisolone

C Give tissue plasminogen activator (tPA)

D Commence ganciclovir

E Commence prostacyclin

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Question 10 of 20

B	Commence methylprednisolone

The patient has acute graft-versus-host disease (GVHD). This presents within 100 days of an allogeneic bone marrow transplantation with a skin rash (can progress to erythroderma), liver dysfunction (cholestatic) and diarrhoea (sometimes bloody). It remains a serious cause of mortality and morbidity among bone marrow transplant recipients.

Patients are staged on the severity of involvement of the skin, liver and gastrointestinal tract. Initial aggressive treatment with intravenous (IV) corticosteroids is recommended. Anti-T cell antibodies, such as OKT3, have been used in patients with resistant disease, as have rituximab and anti-thymocyte globulin.

A	Stop ciclosporin

Ciclosporin should not be stopped, unless levels are considered in the

Ciclosporin should not be stopped, unless levels are considered in the toxic range.

C Give tissue plasminogen activator (tPA)

tPA is most useful in veno-occlusive disease associated with bone marrow transplantation.

D Commence ganciclovir

There is no evidence that the skin lesions are related to cytomegalovirus (CMV); as such, ganciclovir is not required here.

E Commence prostacyclin

Like tPA, prostacyclin is useful in veno-occlusive disease associated with stem cell transplantation because it leads to small vessel dilatation.

33300

Question 11 of 20

A 73-year-old man with a history of ischaemic heart disease has been treated with cyclophosphamide and prednisolone for myeloma, diagnosed some time ago.

Over the past two follow-up visits, there has been a gradual rise in his free light chain excretion and an increase in his creatinine from 122 to 142 µmol/l. His blood pressure (BP) is well controlled at 142/70 mmHg on amlodipine 5 mg.

Which of the following interventions is most likely to prevent further renal deterioration?

A ACE inhibition

B Fluid intake ≥3 l/day

C Low-phosphate diet

D Low-salt diet

E Spironolactone

A 73-year-old man with a history of ischaemic heart disease has been treated with cyclophosphamide and prednisolone for myeloma, diagnosed some time ago.

Over the past two follow-up visits, there has been a gradual rise in his free light chain excretion and an increase in his creatinine from 122 to 142 µmol/l. His blood pressure (BP) is well controlled at 142/70 mmHg on amlodipine 5 mg.

Which of the following interventions is most likely to prevent further renal deterioration?

Your answer was correct

A	ACE inhibition
B	Fluid intake ≥3 l/day
C	Low-phosphate diet
D	Low-salt diet

B	Fluid intake ≥3 l/day

In the majority of cases, renal impairment is caused by the accumulation and precipitation of light chains, which form casts in the distal tubules resulting in renal obstruction. In addition, myeloma light chains are also directly toxic to proximal renal tubules, further adding to renal dysfunction. Adequate hydration, correction of hypercalcaemia and hyperuricaemia and anti-myeloma therapy should be initiated promptly.

Renal function is optimised by maintenance of a high fluid intake (≥3 l/day), according to the results of the MRC myeloma trial from 1984 (see weblink below). This advice still holds (Myeloma guidelines, 2010), and all patients should be instructed as to the importance of this throughout the course of the disease. Potentially nephrotoxic drugs, including aminoglycosides and non-steroidal anti-inflammatory drugs (NSAIDs), should be avoided.

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Because BP is relatively well controlled on amlodipine, a second antihypertensive agent is not indicated. Moreover, the introduction of an ACE inhibitor could potentially deteriorate his renal function.

C	Low-phosphate diet

This is recommended in advanced stages of kidney disease.

D	Low-salt diet

This is recommended in hypertension and heart failure. In the present scenario, the key advice in order to maintain/improve renal function is adequate fluid intake.

E	Spironolactone

There is no indication for spironolactone in the current scenario; in addition, it is contraindicated for eGFR <30%.

A 23-year-old plumber presents with gum swelling and drowsiness. Previously fit and well, he first noticed some bleeding from his gums, coupled with easy bruising, over the last week. He takes no medications, smokes 10 cigarettes daily and drinks within 21 units per week.

On examination, he has markedly swollen gums, several enlarged lymph nodes in the neck and groin and 3 cm hepatosplenomegaly. Basic observations were unremarkable. Fundoscopy reveals several retinal haemorrhages and dilated retinal veins.

Investigations:

Hb	6.3 g/dl
WCC	353.7 × 10^9/l
PLT	6.0 × 10^9/l
Blood film	Heavy infiltrate of blasts with monocytoid features
Serum lysozyme	73 mg/l (4–13)

lysozyme	73 mg/l (4–13)
APTT	45 s (30–40)

What is the most appropriate treatment?

A	Combination chemotherapy including arabinosylcytosine after apheresis
B	Transfusion of two units of irradiated blood after apheresis
C	Transfusion of two units of non-irradiated, cytomegalovirus-negative blood before apheresis
D	All-trans-retinoic acid
E	Dexamethasone and vincristine combination chemotherapy

Question 12 of 20

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APTT	45 s (30–40)

What is the most appropriate treatment?

Question 12 of 20

A	Combination chemotherapy including arabinosylcytosine after apheresis

This patient has acute myeloid leukaemia (AML) of either subtype M4 (myelomonocytic) or M5 (monocytic). AML M4/5 are characterised by gum infiltration, organomegaly and lymphadenopathy, monocytoid blasts and raised serum lysozyme. Hypokalaemia and coagulopathy are common. Chemotherapy regimens are designed to achieve induction, (attaining remission), followed by post-remission consolidation, (intensification). Regimes commonly include arabinosylcytosine, mitoxantrone and daunorubicin. The patient also has leucostasis/hyperviscosity, with a high white cell count, drowsiness and retinal vein dilation. Even though he is significantly anaemic, blood transfusion in this situation can cause rapid deterioration and should be done after the white cell count has been brought under control – often blood is

Question 12 of 20

brought under control – often blood is transfused during therapeutic apheresis.

B	Transfusion of two units of irradiated blood after apheresis

Irradiated blood products are used to prevent transfusion-associated graft-versus-host disease in patients with suppressed cellular immunity (Hodgkin's disease, purine analogue therapy and post-stem cell transplant).

C	Transfusion of two units of non-irradiated, cytomegalovirus-negative blood before apheresis

Transfusion of blood before apheresis in a patient with hyperviscosity runs the risk of precipitating rapid deterioration due to an acute thrombosis.

D	All-trans-retinoic acid

Question 12 of 20

Transfusion of blood before apheresis in a patient with hyperviscosity runs the risk of precipitating rapid deterioration due to an acute thrombosis.

D	All-trans-retinoic acid

All-trans-retinoic acid is used in AML M3 (acute promyelocytic leukaemia), where high white cell counts are the exception, lysozyme is not raised and organomegaly and gum hypertrophy are not usual.

E	Dexamethasone and vincristine combination chemotherapy

These agents are used to induce remission in acute lymphoblastic leukaemia.

33290

Rate this question:

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A 45-year-old self-employed painter and decorator who specialises in renovating old houses is referred to the Haematology Clinic complaining of lethargy and tiredness.

His GP has checked a blood sample and found that he is anaemic, with an Hb of 101 g/l. In addition, the film is commented on and is said to contain polychromatophilic, stippled red blood cells. MCV is 69 fl and serum ferritin is reported as normal.

Which of the following diagnoses fits best with this clinical picture?

A Ethanol abuse

B Thalassaemia

C Lead poisoning

D Myelodysplasia

E Myelofibrosis

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Which of the following diagnoses fits best with this clinical picture?

Your answer was correct

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B Thalassaemia

C Lead poisoning

D Myelodysplasia

E Myelofibrosis

Explanation

C Lead poisoning

C Lead poisoning

There is a major clue in the occupation of this gentleman, in that he may have been exposed to significant quantities of lead in his occupation renovating old buildings. Whilst lead-containing paint was discontinued some years ago, it is still found in older properties. Lead poisoning is a cause of sideroblastic anaemia, characterised by microcytosis, polychromatic, stippled red blood cells and ring sideroblasts with erythroid hyperplasia on bone marrow examination. Elimination of lead exposure in this case may lead to a slow recovery.

A Ethanol abuse

The direct toxic effects of alcohol can lead to sideroblastic anaemia, although it seems perhaps unlikely with a significant alcohol addiction that he would be able to hold down his job as a painter and decorator.

B Thalassaemia

B Thalassaemia

Thalassaemia does result in microcytic anaemia, although it also leads to elevated iron and ferritin, and many other features of chronic disease not seen here.

D Myelodysplasia

The blood film is not typical for myelodysplasia. The blood film characteristically shows dimorphic red cells, with Pappenheimer bodies, basophilic stippling and dysplastic erythrocytes, as evidenced by anisocytosis and poikilocytosis.

E Myelofibrosis

Given the age of this patient, myelofibrosis is very unlikely; in addition, teardrop-shaped red blood cells and a leucoerythroblastic blood picture are more usual features.

18536

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The following panel results were seen for a transfusion recipient and the donor unit of blood.

Donor sample is positive for the following antibodies;

Anti A positive
Anti B positive
Anti rhesus positive

Recipient is positive for the following antibodies;

Anti-A positive
Anti-B negative
Anti rhesus negative

What blood group was the recipient?

A AB-
B B+
C A+
D A-
E B-

Question 14 of 20

B	B+

This man has antibodies to the A blood group antigen, which means he does not possess it himself. In contrast, he has no anti-B or anti-rhesus antibodies, and therefore he must have a B+ blood group. The donor panel suggests that the donor has antibodies to all three antigens, A, B and rhesus. As such, he or she must be blood group O–, the so-called universal donor.

A	AB-

The presence of anti-A antibodies means this patient’s red cells cannot carry the A antigen. Blood groups B or O may be associated with anti-A antibodies.

C	A+

The presence of anti-A antibodies means this patient’s red cells cannot carry the A antigen.

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C	A+

The presence of anti-A antibodies means this patient's red cells cannot carry the A antigen.

D	A-

Anti-A antibodies rule out the presence of the A blood group antigen. The fact that the recipient is anti-rhesus negative means that his blood cells must carry the rhesus antigen.

E	B-

Although the fact he is anti-A positive would fit with the B blood group, anti-rhesus negativity fits with his red cells carrying the rhesus antigen.

20997

Rate this question: ☆☆☆☆☆

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A 38-year-old motorcyclist is admitted to the Emergency Department. It quickly becomes apparent that he has suffered an unstable pelvic fracture during his accident and is gravely ill.

The Emergency Department staff carry out blood testing, and his Hb is revealed as 40 g/l. He confirms that he is of sound mind and that he is a Jehovah's witness, his religion meaning that he should refuse a blood transfusion. He later dies.

To which of the following ethical principles should the treating physician refer in explaining his reasons for not carrying out a transfusion?

A	Autonomy
B	Beneficence
C	Non-maleficence
D	Justice

Question 15 of 20

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D	Justice
E	Utilitarianism

20995

Question 15 of 20

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To which of the following ethical principles should the treating physician refer in explaining his reasons for not carrying out a transfusion?

Your answer was incorrect

A Autonomy

B Beneficence

Question 15 of 20

A Autonomy

In the case of a competent adult, patient autonomy must be respected as being of utmost importance, and patient beliefs related to being a Jehovah’s Witness are an example of where autonomy must be supported.

E Utilitarianism

Utilitarianism is essentially the principle of doing the ‘greatest good for the greatest number’. Utilitarianism may have applied if the doctor had treated a man who had a number of dependants, and was under-insured, making an argument that preserving this man’s life had a much wider benefit (although at the time of injury this is of course highly unlikely to be apparent!).

B Beneficence

This is the medical principle that any

this is of course highly unlikely to be apparent!).

B	Beneficence

This is the medical principle that any treatment intervention must be for the benefit of the patient.

C	Non-maleficence

Non-maleficence is the principle of ‘first do no harm’ when initiating patient treatments.

D	Justice

In medical ethics, the concept of justice can be subdivided into three categories: fair distribution of healthcare resources (distributive justice), respect for people's rights (rights based justice) and respect for the law (legal justice).

20995

Rate this question: ⊖ ☆☆☆☆☆

Question 16 of 20

You are asked to see a 20-year-old man with a temperature of 39 °C. He is an in-patient receiving an allogeneic bone marrow transplant. He was diagnosed with chronic myeloid leukaemia three months previously and was treated with imatinib mesylate, which brought about a rapid haematological and cytogenetic remission.

He received myeloablative conditioning with total body irradiation and cyclophosphamide 10 days previously, and received stem cells collected from his brother, with whom he is fully HLA (human leucocyte antigen) compatible. He first became febrile five days ago, and has received ceftazidime (changed to meropenem after 48 h) and vancomycin intravenously.

Examination shows an unwell young man; pulse 120 beats per minute, blood pressure 110/60 mmHg, heart sounds normal; capillary refill < 2 s; respiratory rate 24 breaths per minute, crackles in the right mid-zone; abdomen normal. Urine output is above 30 ml/h, and has

the right mid-zone, abdomen normal. Urine output is above 30 ml/h, and has been negative to date.

Investigations:

Hb	9.3 g/dl
WCC	0.2 x 10^9/l
PLT	12 x 10^9/l
Blood cultures	- at 48 h
Urine cultures	- at 48 h
Chest X-ray	Right middle lobe patchy consolidation

What is the most appropriate management?

A	Add in metronidazole for anaerobic cover
B	Change vancomycin to linezolid to cover vancomycin resistant enterococcus

Chest X-ray	Right middle lobe patchy consolidation

What is the most appropriate management?

A Add in metronidazole for anaerobic cover

B Change vancomycin to linezolid to cover vancomycin resistant enterococcus

C Add in acyclovir 10 mg/kg to cover systemic herpes infection

D Add in liposomal amphotericin 3 mg/kg to cover invasive aspergillosis

E Add in intravenous fluconazole 400 mg daily to cover invasive candidiasis

Question 16 of 20

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Blood cultures	- at 48 h
Urine cultures	- at 48 h
Chest X-ray	Right middle lobe patchy consolidation

What is the most appropriate management?

Your answer was incorrect

D Add in liposomal amphotericin 3 mg/kg to cover invasive aspergillosis

The gravest concern is that the fevers are due to invasive aspergillosis (IA) or related fungal infection. Systemic herpes infection or candidiasis are both possible, but less likely. Diagnosing IA is difficult; computed tomography of the chest is useful at identifying lesions, but is not completely sensitive or specific. Bronchoscopy with lavage suffers from the same limitations, and invasive procedures are discouraged in neutropenic patients. Various serological assays have been trialled, including using the polymerase chain reaction to detect early invasive disease. IA can only be confidently diagnosed by the finding of characteristic hyphae on a biopsy specimen, but for obvious reasons this is rarely available. Vorconazole is the treatment of choice followed by posaconazole. Amphoteracin is used if neither of these agents is effective.

Question 16 of 20

treatment of choice followed by posaconazole. Amphoteracin is used if neither of these agents is effective. Caspofungin, micafungin and anidulafungin can be used if first-line agents are either ineffective or not tolerated. Any immunosuppressive drugs may be reduced, or granulocyte-stimulating colony factor can be used to rectify neutropenia whilst a patient is unwell

B Change vancomycin to linezolid to cover vancomycin resistant enterococcus

VRE would only be considered at this point if there was microbiological evidence.

A Add in metronidazole for anaerobic cover

The patient has been well treated for neutropenic sepsis and meropenem will provide reasonable anaerobic cover, so metronidazole is not

Question 16 of 20

neutropenic sepsis and meropenem will provide reasonable anaerobic cover, so metronidazole is not required.

C	Add in acyclovir 10 mg/kg to cover systemic herpes infection

Although systemic herpes infection is possible, it is less likely than other infections such as fungal infections and, as such, would not be the next step in treatment.

E	Add in intravenous fluconazole 400 mg daily to cover invasive candidiasis

Invasive candidiasis should be a consideration but is less likely to be the cause of the ongoing symptoms than invasive aspergillosis and treatment of candidiasis would, therefore, not be the next step.

6300

Rate this question:

A 49-year-old white woman presents to a locum GP to find out the results of some blood investigations performed by her own GP.

She was found to have splenomegaly on a routine examination when she visited her GP, with feelings of excessive tiredness and fatigue. Her blood film had shown elevated basophils and eosinophils with poikilocytes and normoblasts.

Investigations:

Hb	11.0 g/dl
WCC	38 × 10^9/l
PLT	119 × 10^9/l

Which diagnosis would fit the above data?

A	Sideroblastic anaemia
B	Chronic myeloid leukaemia
C	Polycythaemia rubra vera

basophils and eosinophils with poikilocytes and normoblasts.

Investigations:

Hb	11.0 g/dl
WCC	38 × 10⁹/l
PLT	119 × 10⁹/l

Which diagnosis would fit the above data?

- A Sideroblastic anaemia
- B Chronic myeloid leukaemia
- C Polycythaemia rubra vera
- D Essential thrombocythaemia
- E Thalassaemia

7641

Question 17 of 20

A 49-year-old white woman presents to a locum GP to find out the results of some blood investigations performed by her own GP.

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PLT	$119 \times 10^9/l$

Which diagnosis would fit the above data?

A	Sideroblastic anaemia
B	Chronic myeloid leukaemia
C	Polycythaemia rubra vera

B Chronic myeloid leukaemia

Chronic myeloid leukaemia (CML) is one of the myeloproliferative disorders and results from an uncontrolled proliferation of myeloid cells. It is an acquired abnormality involving the haematopoietic stem cell and a reciprocal chromosomal translocation, resulting in the Philadelphia (Ph) chromosome. This chromosome is present in the granulocyte, RBC and platelet precursors of >95% of patients with CML. Poikilocytes are variably shaped erythrocytes. Of the conditions listed, the only one which would cause such a marked elevation of the WCC, thrombocytopenia and mild anaemia is CML.

A Sideroblastic anaemia

Sideroblastic anaemia is associated with the formation of ring sideroblasts, because of defective incorporation of iron into red blood cells.

C Polycythaemia rubra vera

PCRV is associated with predominant elevation in haemoglobin, rather than the marked elevation in white count seen here.

D Essential thrombocythaemia

Essential thrombocythaemia is primarily associated with an increase in platelet count, rather than the increase in white count seen here.

E Thalassaemia

Thalassaemia would not account for the marked elevation in white count with immature red blood cells seen on the film here.

7641

A 30-year-old man presents with breathlessness on exertion of 3 months' duration. He is usually fit and relatively athletic and now needs to stop for breath on climbing a single flight of stairs.

His general practitioner has arranged investigations for possible renal stones, and he completed a 6-month course of warfarin for deep vein thrombosis (DVT) in the last year, but otherwise he has no significant previous medical history.

Examination shows pale conjunctivae and a pulse of 100 bpm; heart sounds are normal, and the jugular venous pressure is not raised.

Investigations:

Haemoglobin (Hb)	6.3 g/dl
White cell count (WCC)	2.5 × 10^9/l
Neutrophils	1.1 × 10^9/l
Platelet	163 × 10^9/l

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Platelet (PLT)	163 × 10^9/l
Mean corpuscular volume (MCV)	80 fl (80–96)
Reticulocytes	90 × 10^9/l (25–85)
Blood film	Marked anisocytosis, with polychromasia and hypochromatic cells
Ferritin	10 µg/l (15–300)
Urine dipstick	Blood+++
Mid-stream urinalysis	No cells
Urine culture	Negative

What is the most likely diagnosis?

A	Warm autoimmune haemolysis

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Urine dipstick	Blood+++
Mid-stream urinalysis	No cells
Urine culture	Negative

What is the most likely diagnosis?

A	Warm autoimmune haemolysis
B	Cold haemagglutinin disease
C	Paroxysmal cold haemoglobinuria
D	Blackwater fever
E	Paroxysmal nocturnal haemoglobinuria (PNH)

6299

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Mean corpuscular volume (MCV)	80 fl (80–96)
Reticulocytes	90×10^9/l (25–85)
	Marked anisocytosis

E	Paroxysmal nocturnal haemoglobinuria (PNH)

This patient has iron deficiency, mild pancytopenia and urine that is positive for Hb but with no red cells seen in the urine. This is most likely to be due to chronic intravascular haemolysis where free circulating Hb is filtered in the kidneys (haemoglobinaemia and haemoglobinuria). A Perl's stain of the urine will be positive due to iron absorption in uro-epithelial cells, which are then shed in the urine. The causes of chronic intravascular haemolysis are chronic micro-angiopathies, particularly chronic disseminated intravascular coagulation (often secondary to prostatic cancer) and PNH.

PNH is characterised by loss of resistance to complement lysis, so that under acidic conditions, red cells are spontaneously lysed. The condition is confirmed by showing loss of PIG-A anchored proteins that confer resistance to complement-mediated lysis – such as DAF (decay accelerating

resistance to complement-mediated lysis – such as DAF (decay accelerating factor) and MIRL (membrane inhibitor of reactive lysis), although in the past, the condition was confirmed with either Ham's or the sucrose lysis test.

This diagnosis is also consistent with previous deep vein thrombosis. PNH is associated with a 40% prevalence of venous thrombosis in the intra-abdominal venous network and is generally prothrombotic. The mechanism for this is poorly understood.

A Warm autoimmune haemolysis

Warm autoimmune haemolytic anaemia (AIHA) is the most common haemolytic anaemia. Usually, patients present with an increased MCV and hyperbilirubinaemia. The direct Coombs test is diagnostic and also tests for antibodies attached to the surface of red blood cells. Treatment is with corticosteroids and

with corticosteroids and immunoglobulins. This patient’s MCV is not in keeping with warm AIHA. Also in AIHA, you would not expect to find Hb in the urine, meaning that AIHA is not the most likely diagnosis for this patient.

B	Cold haemagglutinin disease

Cold haemagglutinin disease is a rare autoimmune haemolytic disease. The cause of the disease is usually unknown in primary disease, but secondary cold agglutinin disease may be associated with certain cancers or viral, bacterial or parasitic infections. Treatment is usually supportive, with any identifiable causes requiring treatment. This patient could potentially have cold haemagglutinin disease. However, this is less likely, given that he did not appear to have a triggering infection, and this diagnosis would not explain pancytopenia, as noted here.

Paroxysmal cold haemoglobinuria is a rare AIHA, characterised by exposure to cold temperatures, leading to Hb in the urine. Triggers include viral and bacterial infections such as measles, mumps, influenza, cytomegalovirus and Epstein–Barr virus. Treatment for the disease itself is not required, as it is usually self-limiting. Antibiotics can be used to resolve bacterial infections.

D	Blackwater fever

Blackwater fever is usually a complication of malaria whereby red blood cells haemolyse, leading to deposition of Hb within the blood vessels and urine. It is associated with pyrexia, jaundice, rapidly progressing anaemia and dark red/black urine. This patient has some features in keeping with blackwater fever, such as dark urine and anaemia, but the anaemia was insidious in onset and he has neither fevers nor any notable travel history and has pancytopenia.

A 57-year-old man is referred to hospital by his GP. Previously well, he gives a history of progressive weakness and breathlessness on exertion over a 2-week period. He is also complaining of symptoms of indigestion. On examination, he is pale and tachycardic. His blood pressure is 110/70 mm Hg. His heart sounds are normal and his chest is clear.

He brings along with him results of blood tests done by his GP:

Hb	8.3 g/dl
WCC	5.2 x 10^9/l
PLT	410 x 10^9/l
MCV	69 fl
Peripheral smear	RBCs hypochromic and microcytic, target cells +, pencil cells +, WBC and platelet morphology normal

Which one of the following would you consider an appropriate next step to

Peripheral smear	microcytic, target cells +, pencil cells +, WBC and platelet morphology normal

Which one of the following would you consider an appropriate next step to measure?

A	Serum iron and total iron-binding capacity (TIBC)
B	Serum ferritin
C	Blood lead level
D	Hb electrophoresis and Hb H preparation
E	Liver function tests

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B Serum ferritin

This patient is most likely to have iron-deficiency anaemia due to gastrointestinal blood loss. Hypoferritinaemia confirms iron deficiency and is the preferred screening test. Ferritin levels may be falsely elevated in acute inflammatory states (ferritin is an acute-phase reactant).

Stool for occult blood is a relatively insensitive test of gastrointestinal bleeding. Malabsorption, hookworm infestation and chronic haematuria may also result in iron deficiency. Other causes of microcytosis include haemoglobinopathy (in certain ethnic groups), anaemia of chronic disease (normal/high ferritin levels), lead poisoning (check urine and blood lead levels) and myelodysplastic syndromes with ringed sideroblasts.

A Serum iron and total iron-binding capacity (TIBC)

In order to properly understand a value

In order to properly understand a value for TIBC, one also must know the serum iron, the percentage transferrin saturation and the individual clinical situation.

In modern laboratory testing, serum ferritin levels are generally accepted as reliable single indicators of the presence of iron deficiency.

C Blood lead level

Acute lead poisoning can cause anaemia through haemolysis, accompanied by haemoglobinuria. There is no evidence in this scenario which would support this diagnosis. Symptoms in chronic lead poisoning usually occur with blood levels greater than 50 µg/dl.

D Hb electrophoresis and Hb H preparation

Haemoglobinopathy is one cause of microcytosis, but it is not the

Symptoms in chronic lead poisoning usually occur with blood levels greater than 50 µg/dl.

D Hb electrophoresis and Hb H preparation

Haemoglobinopathy is one cause of microcytosis, but it is not the commonest and it is usually discovered earlier in life.

E Liver function tests

There is no evidence of liver disease from the history and clinical examination, and therefore liver function testing would not be essential for the diagnosis.

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Question 20 of 20

A 26-year-old nurse who has experienced anaphylaxis after eating a fruit salad is recovering in the Emergency Department. She was treated with IV hydrocortisone, antihistamines and IM adrenaline. This is the first occasion that she has had an allergic reaction to fruit.

Her BP is now 122/72 mmHg, with pulse 80/min and regular. Her chest is clear, O_2 saturations are 95%.

Which of the following is the most appropriate observation time prior to discharge?

A 4 hrs
B 6 hrs
C 8 hrs
D 12 hrs
E 24 hrs

D 12 hrs

Anaphylaxis is the result of immunoglobulin E-mediated mast cell degranulation, which releases inflammatory immune mediators. These mediators cause increased vascular permeability, peripheral vasodilation, increased mucus production and bronchial smooth muscle contraction. Anaphylactoid reactions do not require a previous exposure to an allergen, but the clinical course and treatment are identical to those of anaphylaxis.

The primary precipitants of anaphylactic reactions are foods (e.g. milk, soy, eggs, nuts and shellfish), medications (e.g. antibiotics [penicillin], non-steroidal anti-inflammatory drugs, anaesthetics), venom (*Hymenoptera* stings), intravenous contrast materials and latex. Up to 20% of anaphylactic reactions are idiopathic.

Patients with severe anaphylactic reactions, particularly of rapid onset, are at risk of biphasic or rebound

reactions, particularly of rapid onset, are at risk of biphasic or rebound anaphylaxis. The recurrence rate is as high as to 20%. The severity of the reaction, the time of onset after exposure to antigen before the occurrence of symptoms of the primary response, the presence of hypotension or laryngeal oedema during the primary response, and previous history of a biphasic reaction have all been mentioned as risk factors. On average the latest these are seen is 8–10 h after the primary reaction; 12 h is therefore sufficient observation time. All patients being sent home from the Emergency Department should have immediate access to epinephrine injections.

C 8 hrs

Although the majority of cases occur before the 8 h time point, some serious second-phase reactions may be missed.

A 4 hrs